Gynecologic Oncology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Society position statements/white papers

Vulvar carcinoma in Norway: A 50-year perspective on trends in incidence, treatment and survival

Christin Julia Meltzer-Gunnes [a,*], Milada Cvancarova Småstuen [b], Gunnar Balle Kristensen [c], Claes Göran Tropé [c], Agnes Kathrine Lie [d], Ingvild Vistad [a]

[a] Department of Obstetrics and Gynecology, Sorlandet Hospital HF, P.O. Box 416, 4604 Kristiansand, Norway
[b] Department of Nursing and Health Promotion, Oslo and Akershus University College of Applied Sciences, P.O. Box 4, St. Olavs plass, 0130 Oslo, Norway
[c] Department of Gynecological Oncology, The Norwegian Radium Hospital, Oslo University Hospital, P.O. Box 4953 Nydalen, 0424 Oslo, Norway
[d] Center for Laboratory Medicine, Ostfold Hospital HF, P.O. Box 300, 1714 Gralum, Norway

HIGHLIGHTS

- The incidence of vulvar carcinoma is increasing, particularly among younger women.
- Recent incidence rates are significantly higher than observed in other countries.
- Despite less radical treatment, survival has improved.

ARTICLE INFO

Article history:
Received 29 December 2016
Received in revised form 28 February 2017
Accepted 10 March 2017
Available online xxxx

Keywords:
Vulvar cancer
Squamous cell carcinoma
Incidence
Survival

ABSTRACT

Objective. To explore trends in vulvar squamous cell carcinoma (SCC) incidence, age and stage at diagnosis, treatment and survival in Norway from 1961 to 2010.

Methods. From 1961 to 2010, 2233 cases of vulvar SCC were extracted from the Cancer Registry of Norway. Data on age at diagnosis, tumor morphology, stage of the disease and treatment were analyzed. Age-standardized incidence rates, adjusted to the Norwegian standard population, were computed. Relative survival was calculated as a ratio of the observed survival in the study population over the expected survival in the background population. Multivariate Cox model was fitted to estimate hazard ratios.

Results. The overall incidence of vulvar SCC increased >2.5 fold (from 1.70 to 4.66 per 100,000 women/year; $P < 0.01$). Age-specific incidence rates increased among women aged ≤60 years (by 150% in age group 0–39 years, 175% in age group 40–49 years and 68% in age group 50–59 years). From 1971 to 2010, the percentage of patients receiving surgery as only treatment decreased from 81% to 61%, whereas the use of radiation and combination therapy (surgery and radiation) increased from 3% to 11% and 6% to 20%, respectively. 5-year relative survival increased significantly among women ≤80 years (from 72% to 83% among women aged ≤60 years and from 60% to 65% among women aged 61–80 years).

Conclusions. The incidence of vulvar SCC has increased since the sixties, particularly among women younger than 60 years. Despite less aggressive surgical treatment, survival has improved.

1. Introduction

Vulvar cancer is a rare disease representing approximately 4% of all female genital cancers, with an incidence of 0.5–1.5 in 100,000 women per year. Squamous cell carcinoma (SCC) is the most common histological type constituting >90% of the cases and a recent, worldwide study reported that approximately 25% of vulvar cancers are associated with human papilloma virus (HPV) infection [1]. Vulvar carcinoma used to primarily affect women older than 65 years [2]. However, several recent, international studies indicate an increasing incidence [3–5], particularly among younger women, possibly due to increased HPV-exposure [6]. Higher stage of the disease and the presence of inguinofemoral lymph node metastases are known to be the most important factors associated with negative outcome [7].

Until the end of the 1980s, en bloc radical vulvectomy with bilateral inguinofemoral lymphadenectomy was the treatment of choice for

* Corresponding author.
E-mail addresses: christin.julia.meltzer-gunnes@sshf.no (C.J. Meltzer-Gunnes), Milada-Cvancarova.smastuen@hioa.no (M.C. Småstuen), gbk@ous-hf.no (G.B. Kristensen), c.g.trope@medisin.uio.no (C.G. Tropé), Agnes.Kathrine.Lie@so-hf.no (A.K. Lie), ingvild.vistad@sshf.no (I. Vistad).

http://dx.doi.org/10.1016/j.ygyno.2017.03.008
0090-8258/

vulvar cancer [8]. Over time, less aggressive local resections were introduced for smaller primary tumors [7] and other (neo)adjuvant treatment modalities including radiation and chemotherapy became available for patients with advanced disease [9,10].

Previous reviews have reported that less aggressive treatment has no detrimental effect on survival [11]. However, findings on trends in survival over the last decades are inconsistent: Improved five-year relative survival rates have been reported in England and the Nordic countries (from 1990–2005 to 1964–2003, respectively) [4,12], while stable survival rates have been demonstrated in the Netherlands and the USA (from 1989–2010 to 1988–2007, respectively) [5,13]. Trends in survival of vulvar SCC patients in Norway have not been investigated after 1990 [14].

Because of the rarity of vulvar cancer, only few population-based studies are published [4,5,7,12,14–18]. Since 1953, all vulvar cancer cases in Norway have been registered in the Cancer Registry of Norway (CRN). The registry is based on the total Norwegian population and has a completeness estimated to be >95% which is achieved by a mandatory reporting by all hospitals, laboratories and general practitioners, in combination with a routine trace-back system [19]. Based on the nearly complete data the CRN uniquely provides, the objective of this article is to give an overview of changes in incidence, age and stage at diagnosis, treatment and survival of vulvar SCC in Norway over the last five decades.

2. Materials and methods

Data on vulvar cancer (International Classification of Diseases Oncology (ICD-O)-10 code C51) was extracted from the CRN for the years 1953–2010. During that period, 3396 invasive vulvar cancers were registered. To assess the HPV-associated burden, we limited the analyses to SCCs. However, we did not examine the different subtypes of squamous cell carcinomas due to incomplete classification, especially before 1990. In total, 2233 cases of vulvar SCC were included for further analyses. For more detailed information, see Fig. 1.

Data concerning patients' age, date of diagnosis and tumor characteristics (topography, histology, stage, treatment, and live/death status) were obtained from the registry. The study period was divided into 10-year intervals and patients were grouped into 3 age categories (≤ 60, 61–80 and ≥81 years of age). Topography and morphology were coded according to the ICD-O [17]. Although ICD—O—3 topographic codes for specific anatomic locations within the vulva are available, most of the cases were coded as vulvar none otherwise specified. Therefore, we could not examine vulvar cancer incidence by anatomic subsites. Cancer was staged according to tumor invasion and status of metastases. Localized cancer was defined as invasive cancer with stromal invasion. Regional cancer was defined as direct extension of tumor into adjacent tissues/organs and/or only regional (groin) lymph node involvement. Distant cancer was defined as distant tumor sites and/or distant lymph nodes involved. Data on treatment was coded as surgery only, radiation only, combination therapy (surgery and radiation), biopsy only and unknown. When analyzing data on treatment modalities, we chose to exclude all cases registered earlier than 1971 ($N = 318$) due to missing information and consequently less reliable data from that early period.

2.1. Statistics

Data were described with counts and percentages. Age-adjusted incidence rates were calculated as the number of cases given the age group and diagnostic period divided by number of females living in Norway at the given period and of given age. Population numbers were retrieved from "Statistics Norway" [20]. Estimates are presented as number of cases per 100,000 women per year. 95% confidence intervals (95% CIs) were constructed as described using normal approximation. Multivariate Cox model was fitted to estimate hazard ratios adjusted for diagnostic period, age and stage of disease. When performing multivariate analyses, we chose to divide patients into two instead of three age categories (≤ 60 and ≥61 years of age), as there was no difference between patients aged 61–80 and ≥81 years. Relative survival was calculated using the actuarial method and the results are expressed as a ratio of the observed survival in the study sample over the expected survival in the background population. In contrary to the multivariate analyses, when performing relative survival analyses, we had to exclude patients with distant disease and all unstaged cases due to small numbers ($N = 81$ (4%) and $N = 88$ (4%), respectively). Furthermore, we excluded cases with negative values for survival time ($N = 2$). P-values <0.05 were considered statistically significant. All tests were two-sided. All analyses were performed using SPSS and Stata.

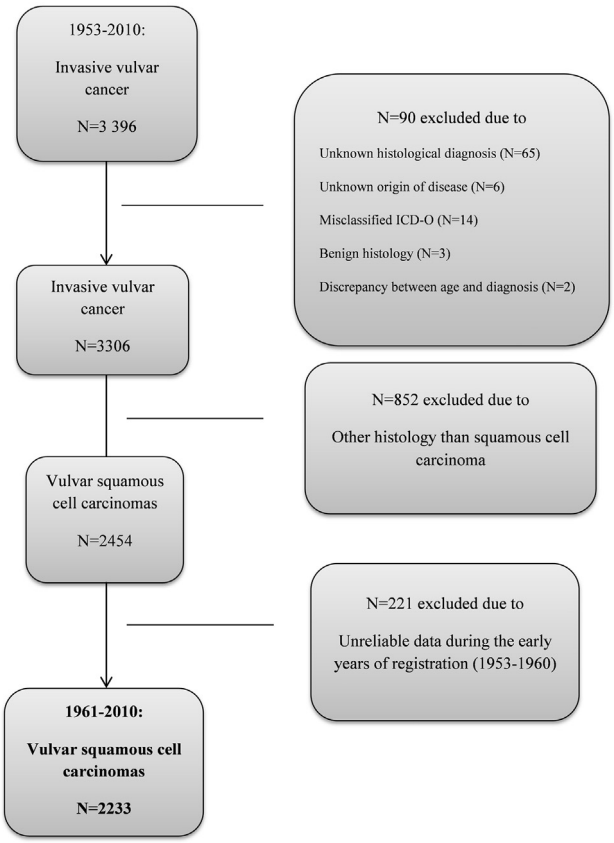

Fig. 1. Included cases of vulvar squamous cell carcinomas, Cancer Registry of Norway.

3. Results

3.1. Incidence and age at diagnosis

Over the last five decades, the age-standardized incidence rate of vulvar SCC has increased >2.5 fold from 1.70 to 4.66 per 100,000 women per year (Table 1, Fig. 2).

Throughout the whole study period, age-specific incidence rates increased with increasing age, with a peak in women aged 80 years and above (Table 1). However, the percentage of women diagnosed with vulvar SCC who were younger than 50 years increased by 75% (from 8 to 14%) from 1961 to 2010 (Table 2). Further, there were statistically significant increases in age-specific incidence rates among women aged ≤60 years, with an increase of 150% in age group 0–39 years, 175% in age group 40–49 years and 68% in age group 50–59 years. A trend towards increasing incidence was also observed in the 60–69 years age group and in those above 80 years. However, these increases did not reach the level of statistical significance. Among

Please cite this article as: C.J. Meltzer-Gunnes, et al., Vulvar carcinoma in Norway: A 50-year perspective on trends in incidence, treatment and survival, Gynecol Oncol (2017), http://dx.doi.org/10.1016/j.ygyno.2017.03.008