

Increasing trends in the incidence of potentially human papillomavirus-related head neck cancers in Italy



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What's new

HPV-driven HNSCCs are rapidly increasing in several Western countries. However, no data exist on the incidence trends of potentially HPV-related and -unrelated HNSCC in Italy. The authors use population-based cancer registry data to depict the evolution in the incidence and survival rates of these malignancies in Italy over a period of 25 years (1988-2012). The trends observed suggest a potential increasing impact of HPV infection on the epidemiology of HNSCC in Italy.

Introduction and objectives

The main risk factors for head and neck squamous cell carcinomas (HNSCCs) are tobacco smoking, alcohol consumption, and HPV infection. HPV-driven HNSCCs are rapidly increasing in several Western countries¹, topographically restricted to the oropharynx², and exhibit a survival benefit compared to HPV-unrelated tumors³. The aim of this study was to explore the incidence trends as well as those in survival rates of HNSCCs arising from different anatomical sites potentially related and unrelated to HPV infection among Italian women and men to provide clues on possible growing impact of HPV in the epidemiology of HNSCC in Italy.

Methods

Epidemiological data were retrieved from 10 long-term Cancer Registries of the Network of Italian Cancer Registries (AIRTUM) covering a population of 7.8 million inhabitants (13% of the whole country) in the period 1988-2012. Trends were described by means of the estimated annual percent change (APC) with appropriate 95% confidence intervals stratified by age and gender, and compared between HPV-related and HPV-unrelated anatomical sites. Only cases with squamous cell histology or morphologic variants of HNSCC were included in the analysis. Cancers arising from lip, nasopharynx, nasal cavity, sinuses, and salivary glands were excluded as they are linked to other etiological factors.

Table. Number of incident cases and age-adjusted incident rate (IR) per 100,000 inhabitants of head and neck squamous cell carcinoma by site and gender during 1988-2012, AIRTUM

Site of HNSCC	Total	Males			Females			IR	
		n	%	IR	n	%	IR		
HPV-related	3984	14.1	1.8	3250	13.8	3.1	734	15.3	0.6
base of tongue	934	3.3	0.4	769	3.3	0.7	165	3.4	0.1
tonsil	2079	7.3	0.9	1655	7.0	1.6	424	8.8	0.4
other oropharyngeal sites	971	3.4	0.4	826	3.5	0.8	145	3.0	0.1
HPV-unrelated									
Oral cavity	7816	27.6	3.3	5277	22.5	5.0	2539	53	1.8
Larynx/hypopharynx	16495	58.3	6.9	14975	63.7	13.8	1520	31.7	1.2
All sites	28295	100	13.8	23502	100	25.0	4793	100	4.2

Statistical analysis

Incidence rates (IR) were reported as European age-standardized and expressed as number of new cases per 100,000 person-year. We assessed the presence of any change in incidence rates through the annual percentage change (APC) statistic with corresponding 95% confidence interval (CI), indicating an increased or decreased trend with a 2-sided P value. The relative survival was calculated for all cases included in the cohort analysis as the ratio of observed to expected survival. National life tables by registry, age, and gender were used for calculating expected survival according to the Ederer II method.

Main strengths and weaknesses in study design

Strengths: the large sample size and the long study period using population-based data in a defined region.
Limits: the lack of individual information about HPV status in tumor tissues and tobacco and alcohol exposure.

Results

A total of 28,295 HNSCCs were included in the analysis (Table). In males, the incidence rate (IR) of cancers arising from sites unrelated to HPV infection significantly decreased in all aged groups (APC: -3.31 for larynx/hypopharynx; APC: -1.77 for oral cavity), whereas stable IR were observed for cancers arising from sites related to HPV infection. In females, IR for cancers from HPV-related sites increased significantly over the observed period with the largest increase in the APC being observed in females aged 60+ (APC: 2.92%), whereas HNSCCs from larynx/hypopharynx significantly decreased in females over 60 years (APC: -0.84) and those arising from the oral cavity significantly increased (APC= 2.15). Five-year relative survival remained largely unchanged in patients with laryngeal/hypopharyngeal SCC and conversely significantly improved in patients with SCC at HPV-related sites (for more details please see Figures 1 and 2).

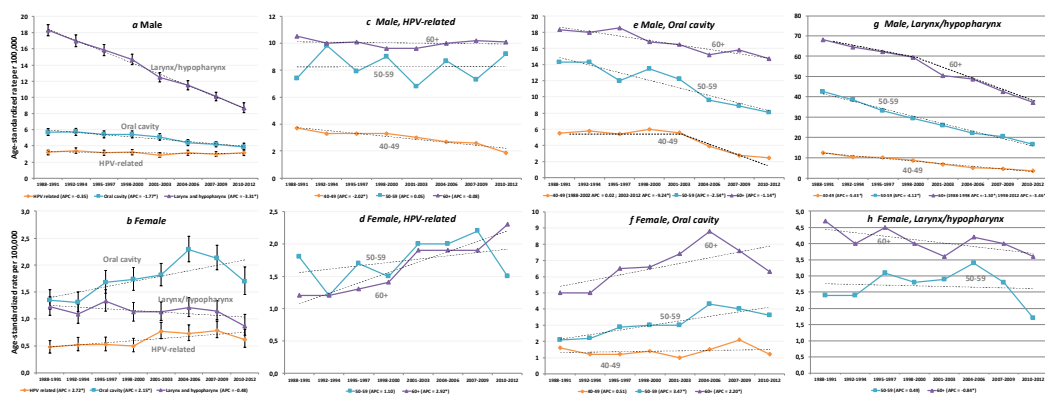


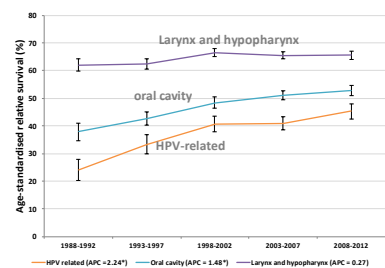
Figure 1. Age-adjusted incidence trends by calendar year of diagnosis for HNSCC by sites.

Panel a and b show a significant decrease in the incidence of HNSCC from HPV-unrelated sites (oral cavity and larynx/hypopharynx) in males, whereas a significant increase was observed in females for HNSCC from oral cavity and a stable trend for HNSCC from larynx/hypopharynx; the incidence of HNSCC from HPV-related sites is significantly increasing in females, whereas it is stable in males; bars indicate confidence interval at 95%. Panel c and d describe the incidence trends in HPV-related HNSCC by age class showing the largest increase in females over 60 years and a decrease in males aged 40-49. Panel e and f show a significant increase in the incidence of oral cavity cancers in females aged over 50 years, whereas a decline was observed in males aged over 40 years. Panel g and h show incidence trends for laryngeal and hypopharyngeal SCCs showing a significant decrease in females over 60 years and a significant decrease in males in all aged groups. The unchanged incidence rate for OPSC observed in males despite the strong reduction registered in environmental-related HNSCC suggests that increasing rates in HPV infection may counterbalance the effects of reduction in tobacco and alcohol exposure. Conversely, in females the net increase in the incidence of SCC at HPV-related sites may result from an increasing role of HPV in these neoplasms in the absence of a substantial environmental-related OPSC reduction.

Anatomical sites related to HPV infection included tonsil (International Classification of Diseases, 10th edition [ICD-10] topography code C09), base of the tongue (C01.9, C02.4), other oropharynx sites (C10), and Waldeyer's ring (C14.2). Anatomical sites unrelated to HPV included the anatomic areas of the oral cavity [tongue (C02 except C02.4), gum (C03), floor of mouth (C04), palate (C05), other and unspecified parts of mouth (C06)] and the laryngeal and hypopharyngeal region [pyriform sinus (C12), hypopharynx (C13), larynx (C32)]. HPV related and HPV-unrelated HNSCC were restricted to squamous cell histology or morphologic variants of SCC (International Classification of Diseases for Oncology, 3rd edition [ICD-O-3] morphology codes 8032, 8033, 8050-8052, 8070-8078, 8082-8084, 8094, 8123) APC annual percent change (star indicates significant difference at P < 0.05)

Figure 2. Five-year age-standardized relative survival by calendar year and HN sites.

Consistently with the hypothesis that the increasing incidence of SCC at HPV-related sites depends on the increasing role of HPV infection, we expected to detect a trend towards an improvement in survival rates of these cancers during the observed period. The figure shows a significantly improved survival in patients with head and neck squamous cell carcinoma arising from human papillomavirus-related sites and from the oral cavity. Conversely, relative survival in patients with laryngeal and hypopharyngeal cancers did not change significantly during the observed period. Expected survival was calculated using the Ederer II method. Age standardized relative survival since diagnosis is the weighted average of age-specific relative survival according to the International Cancer Survival Standard. Bars indicate confidence interval at 95%. APC annual percent change (star indicates significant difference at P < 0.05)



CONCLUSION

Although to a lesser extent and with a different pattern than that observed in other Western countries, the trends in the incidence of HNSCC seen in the present investigation as well as those in survival rates at different sites suggest a potential increasing impact of HPV infection in oropharyngeal oncogenesis in Italy. As, besides cervical cancer, HPV is causally related with other anogenital cancers in both females and males, HPV cancer burden can be reduced if primary and secondary prevention strategies are prioritized in both genders. Thus, every efforts should be made to reinforce the compliance to HPV vaccination programs.