



Effect of previous history of cancer on survival of patients with a second cancer of the head and neck



Jérémie Jégu^{a,b,q,*}, Aurélien Belot^{c,d}, Christian Borel^e, Laetitia Daubisse-Marliac^{f,g,q}, Brigitte Trétarre^{h,q}, Olivier Ganry^{i,q}, Anne-Valérie Guizard^{j,q}, Simona Bara^{k,q}, Xavier Troussard^{l,q}, Véronique Bouvier^{m,q}, Anne-Sophie Woronoff^{n,q}, Marc Colonna^{o,q}, Michel Velten^{a,b,p,q}

^a Registre des cancers du Bas-Rhin, Laboratoire d'Épidémiologie et de Santé Publique, EA3430, FMST, Université de Strasbourg, 4 rue Kirschleger, 67085 Strasbourg CEDEX, France

^b Service de santé publique, Hôpitaux Universitaires de Strasbourg, 1 place de l'hôpital, 67091 Strasbourg CEDEX, France

^c Service de Biostatistique, Hospices Civils de Lyon, 162 avenue Lacassagne, F-69003 Lyon, France

^d Département des maladies chroniques et traumatismes, Institut de Veille Sanitaire, F-94410 Saint-Maurice, France

^e Service d'oncologie médicale, Centre Paul Strauss, 3 rue de la porte de l'hôpital, 67000 Strasbourg, France

^f Registre des cancers du Tarn, 1, rue Lavazière, BP 37, 81001 Albi cedex, France

^g Institut Claudius Regaud, IUCT-O, Registre des Cancers du Tarn, Toulouse F-31059, France

^h Registre des tumeurs de l'Hérault, Centre de Recherche, 208 rue des Apothicaires, 34298 Montpellier CEDEX 5, France

ⁱ Registre des cancers de la Somme, Service Épidémiologie Hygiène et Santé Publique, CHU Nord, 80054 Amiens CEDEX 1, France

^j Registre général des tumeurs du Calvados, Cancers & Préventions – U 1086 Inserm, Centre François Baclesse, Avenue du Général Harris BP 5026, 14076 Caen CEDEX 05, France

^k Registre des cancers de la Manche, Centre Hospitalier Public du Cotentin, 46 rue du Val de Saire, 50102 Cherbourg-Octeville, France

^l Registre des hémopathies malignes de Basse-Normandie, Unité Fonctionnelle Hospitalo-Universitaire n° 0350, Centre Hospitalier Universitaire, Avenue de la Côte de Nacre, 14033 Caen CEDEX, France

^m Registre des tumeurs digestives du Calvados, Cancers & Préventions – U 1086 Inserm, Centre François Baclesse, Avenue du Général Harris BP 5026, 14076 Caen CEDEX 05, France

ⁿ Registre des tumeurs du Doubs et du Territoire de Belfort, EA3181, Centre Hospitalier Universitaire, 25000 Besançon, France

^o Registre des cancers de l'Isère, CHU de Grenoble, Pavillon E BP 217, 38043 Grenoble CEDEX 9, France

^p Service d'épidémiologie et de biostatistique, Centre Paul Strauss, 3 rue de la Porte de l'hôpital, 67065 Strasbourg CEDEX, France

^q Francim: Réseau français des registres des cancers, Toulouse F-31073, France

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SUMMARY

Objective: To provide head and neck squamous cell carcinoma (HNSCC) survival estimates with respect to patient previous history of cancer.

Materials and methods: Data from ten French population-based cancer registries were used to establish a cohort of all male patients presenting with a HNSCC diagnosed between 1989 and 2004. Vital status was updated until December 31, 2007. The 5-year overall and net survival estimates were assessed using the Kaplan–Meier and Pohar-Perme estimators, respectively. Multivariate Cox regression models were used to assess the effect of cancer history adjusted for age and year of HNSCC diagnosis.

Results: Among the cases of HNSCC, 5553 were localized in the oral cavity, 3646 in the oropharynx, 3793 in the hypopharynx and 4550 in the larynx. From 11.0% to 16.8% of patients presented with a previous history of cancer according to HNSCC. Overall and net survival were closely tied to the presence, or not, of a previous cancer. For example, for carcinoma of the oral cavity, the five-year overall survival was 14.0%, 5.9% and 36.7% in case of previous lung cancer, oesophagus cancer or no cancer history, respectively. Multivariate analyses showed that previous history of cancer was a prognosis factor independent of age and year of diagnosis ($p < .001$).

Conclusion: Previous history of cancer is strongly associated with survival among HNSCC patients. Survival estimates based on patients' previous history of cancer will enable clinicians to assess more precisely the prognosis of their patients with respect to this major comorbid condition.

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Abbreviations: SPC, second primary cancer; HNSCC, head and neck squamous cell carcinoma; OS, overall survival; NS, net survival; HR, Hazard ratios; 95% CI, 95% confidence interval; m, months; y, years; ref, reference category.

* Corresponding author at: Laboratoire d'Épidémiologie et de Santé Publique, Faculté de Médecine, Université de Strasbourg, 4 rue Kirschleger, 67000 Strasbourg, France. Tel.: +33 (0)3 68 85 40 26; fax: +33 (0)3 68 85 31 89.

E-mail address: jeremie.jegu@unistra.fr (J. Jégu).

Introduction

With improvements in cancer survival due to earlier detection and advances in cancer treatments, cancer survivors face an increasing risk of developing second primary cancer (SPC) [1]. In particular, patients with a first cancer related to tobacco and

alcohol exposure (such as lung, oesophagus, head and neck cancers) are at greater risk of developing a SPC of the head and neck compared with the general population [2,3]. Most of these SPCs are head and neck squamous cell carcinomas (HNSCC), a type of cancer treated mainly by radiotherapy, surgery and, more recently – for locally advanced disease – chemo radiotherapy or induction chemotherapy followed by radiotherapy based on patient prognosis [4].

However, currently available HNSCC survival estimates may be inappropriate for patients with a HNSCC occurring as a SPC. Indeed, in survival studies based on cancer registry data it is often the practice to restrict the analysis to first primary tumors and to exclude all subsequent primary cancers [5,6]. A more recent approach consists in the inclusion of all primary cancers, irrespective of whether other cancers of a different type have been diagnosed previously in a patient (i.e. patients who had more than one type of cancer are included in different counts) [7,8]. However, these approaches do not consider the history of cancer on survival as, either second HNSCC are excluded, or the estimates of the survivals of patients with a HNSCC occurring as a first or second primary are mixed.

Even if some studies assessed the impact of SPC occurrence on the survival of patients with a first HNSCC [9–12], the survival of patients with a HNSCC diagnosed as a second cancer remains poorly documented. This is a matter of concern as previous history of cancer constitutes one of the major comorbid conditions that can impact HNSCC patients' prognosis and therapeutic management [13].

Using population-based data from France, where the risk of second HNSCC is particularly high [3], the objective of this study was to provide HNSCC survival estimates with respect to patient previous history of cancer. Moreover, the effect of covariates on survival was assessed, including the length of time between the first cancer and the HNSCC diagnosis.

Material and methods

Data from ten French population-based cancer registries belonging to the Francim cancer registries network were used to establish a cohort of all male patients diagnosed with HNSCC between 1989 and 2004. These registries cover eight administrative regions of France (Bas-Rhin, Calvados, Doubs, Hérault, Isère, Manche, Somme and Tarn), which comprise six million inhabitants, or 9.6% of the mainland French population. Quality of data was checked both at the registry level and for the whole common database of Francim. These registries have a high degree of case ascertainment completeness and incidence data are regularly included in the 'Cancer Incidence in Five Continents' monograph series [14]. Moreover, data from these registries were recently used to assess second primary cancer incidence [3] and cancer survival in France [15,16].

Invasive squamous cell carcinomas (*International Classification of Diseases for Oncology*, 3rd edition (ICD-O-3) histology codes 80,703–80,763, 80,783) [17] localized at the oral cavity, oropharynx, hypopharynx and larynx (ICD-O-3 site codes C01–C06, C09–C10, C12–C13 and C32, respectively) were included. Oesophagus, colorectum, lung, prostate and bladder cancers were defined in accordance with topography and morphology codes used in the EURO-CARE project [5]. Included patients could present with a previous history of HNSCC, but not of the same subsite (i.e. oral cavity, oropharynx, hypopharynx and larynx), in compliance with the International Agency for Research on Cancer registration rules, which recommends to not record second primary cancers occurring in the same site than a first cancer if the histology is similar [18]. All available data on invasive cancer cases diagnosed before 1989 were used to define previous history of cancer. The cancer registries were established between 1975 and 1983 (i.e. at least five years before 1989), with the exception of the Manche cancer registry, set up in 1994.

The study concentrated on male patients, as the incidence of HNSCC is scarce among females (incidence rates were of 5 per 100,000 inhabitants in 1995 among females compared with 45 per 100,000 among males [19]), which did not allow reliable estimates of survival with respect to previous history of cancer. Finally, tumor stage, tobacco or alcohol consumption and cancer treatments were not analyzed because detailed data about these exposures were not available. Third- and higher ranked tumors, although not excluded, were not particularly analyzed.

An active follow-up for vital status at December 31, 2007 was carried out for all HNSCC diagnosed between January 1, 1989 and December 31, 2004 using a single standardized procedure, as previously reported [15,16]. Survival time began at date of HNSCC diagnosis (diagnosed as a first or second cancer) and ended at the date of death, last known vital status or December 31, 2007, whichever came first. The proportion of patients with an HNSCC lost to follow-up (i.e. alive at some date before December 31, 2007) was 1.1%.

Firstly, 5-year overall survival was assessed using the Kaplan–Meier estimator. Estimates were stratified by whether patient had previous cancer, previous cancer site and age group (≤ 54 y, 55–64 y, ≥ 65 y). Secondly, net survival was computed using the Pohar-Perme estimator of the net cumulative rate [20]. This estimate corresponds to hypothetical survival in which patients could only die from their cancer; i.e. rates of death from other causes, as given in the general population life tables, are removed. Under its assumptions, net survival can be considered as an estimate of cancer-specific survival. The life tables were available by gender, age, calendar year and French administrative region. Finally, multivariate Cox regression models were used to assess the cancer history effect while adjusting for age and year of HNSCC diagnosis. Adjustment on the other comorbidities (e.g. chronic pulmonary or cardiovascular diseases) could not be performed because such detailed data were not available in this population-based study. Hazard ratios (HR) and their respective 95% confidence intervals (95% CI) were provided by these models. The effect of time of first primary to HNSCC diagnosis on survival was assessed in patients with a previous history of cancer. All analyses were performed using Stata (version 12.1, Stata Corp, College Station, Texas, USA), with the *stns* package for net survival estimates [21].

Results

Among the cases of HNSCC included, 5553 were localized in the oral cavity, 3646 in the oropharynx, 3793 in the hypopharynx and 4550 in the larynx. Patients' characteristics by site are presented in Table 1. Overall mean age at HNSCC diagnosis was 60 y-old. It is remarkable that 11.0–16.8% of patients presented with a history of cancer according to tumor site. The median length of time between the two cancers ranged from 20.6 to 36.4 months, depending on HNSCC site. Among these patients, previous HNSCC, lung cancer or oesophagus cancer were more frequently reported.

Overall 5-year survival estimates are presented in Tables 2–5 for patients diagnosed between 1989 and 2004 with a cancer of the oral cavity, oropharynx, hypopharynx and larynx, respectively. Generally speaking, patients with an HNSCC of the larynx presented the highest 5-year survival (47.6%), followed by patients with a cancer of the oral cavity (34.0%), oropharynx (29.7%) and hypopharynx (23.5%).

Striking differences in patient's prognosis were observed, depending on the type of previous cancer. For example, as reported in Table 2, the survival of patients with a cancer of the oral cavity was greatly reduced among patients with a previous history of HNSCC (5-year survival ranging from 17.2% to 27.4%, depending on HNSCC site), lung cancer (14.0%) or oesophagus cancer (5.9%), compared with patients with no previous history of cancer (36.7%).

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