About invasive cervical cancer: a French population based study between 1998 and 2010

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A R T I C L E   I N F O

A B S T R A C T

Objectives: The new French cancer plan provides the implementation of organized screening. To make an assessment of the situation, we aim to describe clinical, tumor and survival characteristics of patients with invasive cervical cancer.
Study design: Data on women suffering from invasive cervical cancer and diagnosed from 1998 to 2010 were provided by the Cote d'Or breast cancer registry. Survival was described using the Kaplan–Meier method and prognostic factors of survival were estimated in a Cox proportional hazard model.
Results: On the whole, 1019 cancers have been collected including 311 (30.5%) invasive ones. The peak incidence was between 40 and 49 years, with an average age of 52 years (SD = 16.4). Cancers were mostly squamous cell carcinoma (80.1%) and diagnosed at a localized stage (53.7%). Only 49% (71/145) of our population were up to date on their Pap smear follow up with lower rates in deprived women. The 5-year survival rate was 62% (15% for women with FIGO stage IV and 91% for women with FIGO stage I) with a median survival of 12.3 years [95% CI: 6.6–NR]. Multivariate analysis showed that risk of death was the highest for group age 50–59 (OR = 4.93; 95% CI: [1.55–15.70]) compared to women aged less than 40, advanced stage (OR = 3.12; 95% CI [1.82–5.35]), and non accurate follow up (OR = 2.81; 95% CI [1.32–5.97]). After cancer diagnosis, no impact of the deprivation index on survival was found.
Conclusion: This study confirms the poor outcome of advanced invasive cervical cancer and the importance of early detection of cervical cancer. Preventive communication should be even more developed and the implementation of a screening program may go through the provision of improved screening tools.

Introduction

In 2012, 3028 new cervical cancers were diagnosed in France, and 1102 women died of this cancer [1]. With a median age of 51 years at diagnosis, cervical cancer affects young women and can lead to serious adverse events such as infertility and impaired sexual quality of life [2]. After breast and thyroid cancers, cervical cancer is the most common cancer in the 15–44 age group of French women [3].

Persistent infection with oncogenic human papillomavirus (HPV) is considered as the main cause of cervical cancer [4]. Other risk factors are precocious intercourse, multiple sexual partners, higher number of pregnancies and smoking. Natural history of cervical cancer is characterized by a slow evolution and the existence of curable pre-cancerous lesions that make it an ideal candidate for screening. French guidelines recommend to perform Pap smear every 3 years after two normal Pap smears after an interval of 1 year [5]. Until now, cervical cancer screening was an individual initiative.

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In France, the widespread implementation of screening since the 1960s, has led to a sharp decline in cervical cancer incidence and mortality. However since the early 2000s, a stage seems to have been reached and 5-year survival rate has been decreasing (68% in 1989–1991 to 64% in 2001/2004) [6]. Early diagnosis and care provision are associated with a good prognosis with a 5-year survival rate higher than 90% in the localized stages [5,7] compared to 17% in metastatic stages [8]. Most of the deaths occur in women with inadequate follow up and with disadvantaged backgrounds. Since 2014, the new French Cancer Plan 2014–2019 [9] aim to reduce those inequalities by implementing a mass cervical cancer screening program.

Only limited recent French epidemiological data on invasive cancers are currently available. Such data are necessary to assess the situation and evaluate the impact of new policies related to mass screening. Using data providing by the only French registry specialized in gynecological cancers, we aim to describe clinical, tumor and survival characteristics of women diagnosed with cervical cancer between 1998 and 2010.

Materials and method

Study population

All women diagnosed with invasive primary cervical cancer, between January 1, 1998 and December 31, 2010 and living in Côte d'Or at that time, were retrospectively selected. Data were provided by the Côte d'Or gynecological registry which is the only French registry specialized in gynecologic cancers. It has been collected comprehensive data invasive cervical cancers since 1982. Data concerning in situ cervical cancers are currently in update. An approval from the national committee (Commission Nationale de l'Informatique et des Libertés) enables the use of data recorded in the registry for medical studies. According to INSEE (Institut National de la Statistique et des Etudes Economiques), Côte d'Or is a French department located in Burgundy including 524 144 inhabitants and 270 930 women. People under 40 represented 49.2% of the individuals in Côte d'Or compared to 49.8% on the national level. Those over the age of 60 represented 23.9% in Côte d'Or compared to 23.2% nationally [10]. The economic situation there is rather more favorable with only 7.3% of unemployed people compared [11] to the national 9.7% in 2011 [12] and with a median income over the national average.

Variables definition

All of the tumors were staged according to the FIGO classification [13]. Stage I, IIa were considered localize, whereas stages IIb, III and IV were considered advanced. Data on histological subtype (squamous, adenocarcinoma and other subtypes), tumor size (≤ 4 cm, >4 cm), lymph node involvement, presence of primary metastases were also collected.

Regarding clinical information, age at diagnosis (<40 years, 40–65 years, >65 years), hormonal status (genital activity, menopause), parity (0, <3, ≥ 3 children) and the date of last Pap smear (≤ 3 years, >3 years) were analyzed.

For all cases of cancer diagnosed, the place of residence was geolocalised with a Geographic Information System (GIS) running on MAPINFO 10.0 and allocated to an IRIS (Ilots Regroupes pour l'Information Statistique), a geographical area defined by INSEE [14]. It is the smallest geographical unit for which census data are known [15]. There are 822 IRIS in the departments. The smallest IRIS is composed of 11 inhabitants, the biggest one is composed of 4771 inhabitants and the average is 1270 inhabitants. The database provided the number of cancer cases diagnosed in an IRIS for the whole period.

The recently published French EDI (European Deprivation Index, FEDI) was used to attribute a social deprivation score to the IRIS [16]. The index consists of five quintiles: from the most favored (quintile 1) to the least favored (quintile 5). It is calculated for each IRIS and composed of ecological variables identified in the best way to reflect individual experience of deprivation. Thus, the FEDI is associated with subjective and objective poverty.

Statistical analysis

Quantitative variables are given as means with standard deviations (SD) and compared using Student t test or non-parametric tests as appropriate. Qualitative variables were described as percentages with 95% confidence intervals and compared using Pearson Chi square test or Fisher test. The percentage of missing given was calculated.

Survival was calculated from the date of diagnosis until the date of death or the date of the last follow-up. The cut-off date for the survival analysis was set on November 1st, 2013. Patients who were alive after the cut-off date were censored. The median follow-up was calculated using the reverse Kaplan–Meier method which is calculated on the same way as the Kaplan–Meier estimate of survival function, but with the meaning of the status indicator reversed [3]. The crude survival rates were calculated using the Kaplan–Meier method and described with their 95% confidence interval. Prognostic factors for survival were determined using a Cox proportional hazard model. All variables with a p-value less than 0.20 in univariate analyses were entered into the multivariate model. Correlations between co-variables were tested for eligible variables. To prevent collinearity, when two variables were significantly correlated, one variable was retained according to its clinical relevance or to the value of the likelihood ratio. Two multivariate models were tested: the first included all patients and the second included only women whose date of last Pap smear was known.

All reported p values were two-sided and the statistical significance level was set at $p < 0.05$. Analyses were carried out using SAS (Statistical Analysis System version 9.3).

Results

Patients characteristics

For the whole study period, a total of 1019 women with cervical cancer were identified, including 311 (30.5%) women with invasive cancers. The characteristics of the patients are reported in Table 1. The median age of the women at diagnosis was 52 years. The peak incidence was in the age group 40–49 years.

Most women (58.5%) were postmenopausal at diagnosis. Among premenopausal patients, three were pregnant. More than half of the women had one or two children (53.2%), 6% were nulliparous. The date of last Pap smear was recorded in 145 medical records: 51% had a Pap smear older than 3 years and then were consistent with French guidelines. In case of accurate follow-up, 38.6% of women were diagnosed with an advanced stage cancer vs. 64.9% when the last Pap smear was older than 3 years ($p = 0.0016$).

The distribution of the women according to FEDI index was as follow: 22.9% belonged to quintile 1, 15.0% to quintile 2, 19.6% to quintile 3, 19.6% to quintile 4 and 22.9% to the most deprived quintile.

Tumor characteristics

The characteristics of tumors are reported in Table 1. The majority of tumors (80.1%) were squamous cell carcinoma; other subtypes were adenocarcinomas (15.1%) and rare histological