INFLUENCE OF SMOKING HABIT ON AGE AT DIAGNOSIS OF BREAST CANCER

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UTICAJ PUŠAČKE NAVIKE NA STAROSNU DOB PACIJENATA U TRENUTKU POSTAVLJANJA DIJAGNOZE KARCINOMA DOJKE

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ABSTRACT

No studies have yet investigated the influence of smoking on age at diagnosis of breast cancer. Therefore, the present study was carried out. This study consisted of 605 females with pathologically confirmed primary adenocarcinoma of the breast and 438 healthy females matched by age. Among our participants, 86 (14.2%) patients and 62 (14.1%) control subjects, respectively, were smokers. Based on a Cox regression model, evidence suggested that smoking status influenced the age at diagnosis of breast cancer ($HR=0.78$, 95% CI: 0.62-0.99, $P=0.040$). After stratification of the patients according to their menopausal status, the same results were obtained. The present study indicated that non-smokers have a lower age at diagnosis in comparison with patients who smoke.

Keywords: Age at diagnosis, breast cancer, smoking Habit

SAŽETAK

Do sada nisu sprovedena istraživanja kojima se ispituje uticaj pušačke navike na starosnu dob u trenutku postavljanja dijagnoze karcinoma dojke. Iz tog razloga je sprovedena ova studija. Studija je sprovedena na 605 ispitanica sa patohistološki potvrđenim primarnim adenokarcinomom dojke, i 438 zdravih ispitanica odgovarajuće starosne dobi. 86 (14.2%) ispitanica u grupi sa potvrđenom dijagnozom, odnosno, 62 (14.1%) iz kontrolne grupe su bile pušači. Prema Cox modelu regresije dokazana je povezanost pušačkog statusa i starosne dobi u trenutku postavljanja dijagnoze karcinoma dojke ($HR=0.78$, 95% CI: 0.62-0.99, $P=0.040$). Treba napomenuti i da su isti rezultati dobijeni nakon stratifikacije ispitanica prema menopauzalnom statusu. Ova studija je pokazala da su nepušači u trenutku postavljanja dijagnoze karcinoma dojke u mlađoj životnoj dobi u odnosu na pušače.

Ključne reči: starosna dob u trenutku postavljanja dijagnoze, karcinom dojke, pušenje

ABBREVIATIONS

SD – standard deviation

HR – hazard ratio

OR – odds ratio

CI – confidence interval

df – Degree of freedom

INTRODUCTION

Breast cancer is a complex multifactorial disease. Thus, genetic and environmental risk factors are involved in its aetiology (1-4). Tobacco use may be one of the few modifiable risk factors for several types of cancers. Although tobacco smoke contains many potentially harmful substances that may act differently and at different stages in the development of cancers, the association between

smoking and breast cancer risk remains unclear (5-11). Moderate or strong associations between smoking and breast cancer risk have been observed in some studies (6-11). Several prospective studies have focused specifically on the association between smoking and breast cancer survival rate, however, the results of these studies are not consistent (12-15).

While a smoking habit is one of the most preventable causes of cancers, based on our knowledge, there is no study that investigates the influence of smoking on age at diagnosis of breast cancer. Therefore, the present study was carried out to study this relationship.

MATERIALS AND METHODS

A total number of 605 patients with pathologically confirmed primary breast adenocarcinoma were recruited from the chemotherapy department of the Nemazi hospital in Shiraz (Fars province, southwest Iran) from September 2008 to June 2011. The mean age at diagnosis of breast cancer (SD; Min-Max; Median) was 45.7 (10.7; 22-83; 45). Age frequency-matched control subjects (438 people) were randomly selected from healthy female blood donors. The mean age of the control group (SD; Min-Max; Median) was 46.7 (10.6; 22-80; 45).

The Iranian population is one of the most heterogeneous populations in the world (16, 17). Therefore, we selected our patients and control subjects from Persian/Muslims (Caucasian) living in the Fars province (southwest Iran).

Family medical history, specifically the incidence of breast cancer (positive, negative), and the smoking status (smoker, non-smoker) of the patients and control subjects were collected via personal interviews. A woman with at least one first-degree relative with breast cancer was considered to have a positive family history. Informed consent was obtained from each subject before being enrolled in the study, and the study was approved by the institutional review board at our department.

The association between smoking status, family history and the risk of breast cancer was assessed by calculating odds ratios (ORs) and 95% confidence intervals (CIs). To determine the effects of smoking status and family history on age at diagnosis of breast cancer, the Kaplan-Meier survival analysis and the Cox proportional hazards regression model were used. In the analysis, breast cancer was defined as the event, and the age at diagnosis was included in the analysis as time to event. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) (version 11.5). A probability of $P < 0.05$ was considered statistically significant.

RESULTS

Among our participants, 86 (14.2%) patients and 62 (14.1%) control subjects, respectively, were smokers. There was no association between smoking status and risk of breast cancer (OR=1.01, 95% CI: 0.71-1.43, $P=0.978$). Like many studies (18), family history significantly differed between patient cases and control subjects (4.6% in cases vs 2.1% in control subjects; OR=2.31, 95%CI: 1.08-4.95, $P=0.031$).

Table 1 shows the distribution of age among newly diagnosed breast cancer patients and control subjects according to their smoking habit. The Kaplan-Meier survival analysis revealed that a smoking habit was associated with age at diagnosis of breast cancer (log rank statistic=4.440, $df=1$, $P=0.035$). A family history of breast cancer was also associated with age at diagnosis of breast cancer (log rank statistic=1.609, $df=1$, $P=0.205$). In the Cox proportional hazards regression model, smoking status and family history were treated as categorical variables. Hazard ratios (HR) and 95% of confidence intervals (CIs) for the categorical variables were estimated. Based on the Cox regression model, there was an association between smoking status and age at diagnosis of breast cancer (HR=0.78, 95% CI: 0.62-0.99, $P=0.040$). This means that non-smokers have a lower age at diagnosis in comparison to patients who smoke. After stratification of the patients according to their menopausal status, the same results were obtained.

DISCUSSION

In the present case-control study, we investigated two associations: 1) the association between smoking habit and breast cancer risk, and 2) the association between smoking habit and age at diagnosis of breast cancer. Although breast cancer has not been previously regarded as a smoking related cancer (5), recent studies have revealed a positive association between tobacco smoke and breast cancer risk (6-11). Based on the present study, there was no significant association between a smoking habit and a risk of breast cancer. This finding is consistent with some reports (see ref. 5) and is not consistent with other reports (6-11).

We found that the association between smoking status and age at diagnosis of breast cancer was significant.

Table 1. Distribution of age among breast cancer patients and control subjects stratified by their smoking status

Smoking status	Breast cancer patients				Control subjects			
	Age at diagnosis (Years)				Current age (Years)			
	n	Mean	SD	Median	n	Mean	SD	Median
Non-Smokers	519	45.4	10.6	44.0	376	46.1	10.5	44.5
Smokers	86	47.7	11.4	47.0	62	50.5	10.1	50.0
Total	605	45.7	10.7	45.0	438	46.7	10.6	45.0

Epidemiological studies have indicated that women who smoke might experience decreased risk of breast cancer as a result of antiestrogenic effects (19). Therefore, it could be concluded that the antiestrogenic effects of tobacco smoke, at least in part, are a mechanism for explaining our present findings.

It should be mentioned that in Iran, breast cancer patients are younger than breast cancer patients in Western countries (3). We know that susceptibility to breast cancer is a multifactorial trait and its risk factors (either genetic components or environmental factors) may differ between populations. Tobacco smoke contains several thousand various compounds that are carcinogenic to humans, and metabolites of tobacco smoke have been found in the breast fluid and tissue of smokers (20, 21). Many of the carcinogenic compounds present in tobacco smoke are substrates of phase I enzymes, represented by the family of cytochrome P450 enzymes (22, 23). Certain genotypes of several genetic polymorphisms in enzymes involved in the metabolism of xenobiotics (such as P450s and antioxidant enzymes) have been suggested to alter the risk of breast cancer (24-27). The inconsistency of the findings between studies might be attributed to differences between population gene pools, environmental factors and the interaction between the two. The main limitations of the present study are the small sample size, the lack of data on duration of smoking and/or passive smoking and possible confounding by other factors, such as diet, including phytoestrogen intake, cannot be excluded. In the future, our present finding should be confirmed by large-scale studies.

Conflict of Interest

The authors have no financial or non-financial competing interests.

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Figure 1. Comparison of age at diagnosis of breast cancer between smokers and non-smokers, after adjustment for family history

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