

RESEARCH ARTICLE

Cigarette Smoking and Breast Cancer: a Case-control Study in Serbia

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Abstract

Background: Despite the fact that breast cancer is the most common female cancer worldwide, more than half of the breast cancer risk factors remained unexplained. The aim of this study was to investigate the association of cigarette smoking with risk of breast cancer. **Materials and Methods:** A case-control study was conducted in the Clinical Centre of Kragujevac, Serbia, covering 382 participants (191 cases and 191 controls). In the analysis of data logistic regression was used. **Results:** Breast cancer risk was significantly increased in those who quit smoking at ≤ 50 years of age (OR=2.72; 95% confidence interval - 95% CI=1.02-7.27) and in those who quit smoking less than 5 years before diagnosis of the disease (OR=4.36; 95% CI=1.12-16.88). When smokers were compared with nonsmokers without passive exposure to smoking, former smoking significantly increased breast cancer risk (OR=2.37; 95% CI=1.07-5.24). Risk for breast cancer was significantly increased in those who quit smoking at ≤ 50 years of age (OR=3.29; 95% CI=1.17-9.27) and in those who quit smoking less than 5 years before diagnosis of the disease (OR=5.46; 95% CI=1.34-22.28). **Conclusions:** These data suggest that cigarette smoking is associated with an elevated risk of breast cancer among former smokers in Serbia.

Keywords: Smoking - breast cancer - risk factor - case-control study - Serbia

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Introduction

Despite the fact that breast cancer is the most common female cancer worldwide, more than half of the breast cancer risk factors remained unexplained (Madigan et al., 1995; Rockhill et al., 1998; Jemal et al., 2011). Smoking as one of the postulated risk factors for breast cancer has been a subject of numerous studies, because it is one of the few factors that could be modified (Hamajima et al., 2002; Gaudet et al., 2013; Hartz and He, 2013; Pirie et al., 2013).

Results of numerous epidemiological studies about the relationship between cigarette smoking and breast cancer risk are inconsistent (International Agency for Research on Cancer, 2004; Braithwaite et al., 2012). The majority of studies have shown a weak positive association (Reynolds et al., 2004; Cui et al., 2006; Rollison et al., 2008; Slattery et al., 2008; Young et al., 2009) or absence of any association (Prescott et al., 2007; Roddam et al., 2007; Lin et al., 2008; Trivers et al., 2009). In some studies even inverse association was found (Gammon et al., 1998; Lash and Aschengrau, 2002). Some studies suggested that an increased risk of breast cancer may be associated with long duration of tobacco use (Conlon et al., 2010; Bjerkaas et al., 2013; McKenzie et al., 2013), or high intensity of smoking (Cui et al., 2006; Conlon et al., 2010; Luo et al., 2011), early age at smoking initiation (Magnusson et al., 2007; Luo et al., 2011), smoking at

least 5 years before first full-term pregnancy (Reynolds et al., 2004) and decreasing years since quitting (Gram et al., 2005; Young et al., 2009).

The results concerning the relationship between passive smoking (environmental tobacco smoke) and breast cancer risk have been more consistent (Lee and Hamling, 2006; Johnson et al., 2011; Reynolds et al., 2009; Gao et al., 2013). While the results from some studies are unconvincing (Pirie et al., 2008; Anderson et al., 2012), the numerous studies suggested an increase in risk with exposure to passive tobacco smoke (Kropp and Chang-Claude, 2002; Slattery et al., 2008; Luo et al., 2011). This association has been stronger for premenopausal compared to postmenopausal women (Hanaoka et al., 2005; Slattery et al., 2008). The purpose of this study was to investigate the association between cigarette smoking and breast cancer risk.

Materials and Methods

Case-control study was conducted in Clinical Centre of Kragujevac (town in central Serbia with about 200,000 inhabitants) between January 2004 and December 2005, and comprised overall 382 participants.

Case group consisted of 191 patients with newly diagnosed and histologically confirmed breast cancer: no one refused to participate. The mean time interval between diagnosis and interview of cases was 2 months.

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All statistical analyses were conducted using the Statistical Package for Social Sciences software (SPSS Inc., version 19.0, Chicago, IL).

Results

Majority of participants (79.6% of cases and 80.7% of controls) were 50 and more years old. Incomplete or complete primary school had 65.4% of cases and 60.7% of controls. About three quarters (75.9% of cases and 70.7% of controls) were manual workers, farmers or housewives and 63.9% of cases and 71.2% of controls lived with partner (Table 1). Postmenopausal were 80.6% of cases and 84.8% of controls.

When passive smokers were included in the reference category, according to adjusted odds ratios (OR), cases and controls did not significantly differ in smoking habit (either current smoker or former smoker), number of cigarettes smoked per day, duration of smoking, age of smoking initiation and smoking before first full-term pregnancy (Table 2). In former smokers adjusted risk for breast cancer was significantly increased in those who quit smoking at ≤ 50 years of age (OR=2.72; 95% confidence interval - 95%CI=1.02-7.27) and in those who quit smoking less than 5 years before diagnosis of the disease (OR=4.36; 95% CI=1.12-16.88).

When smokers were compared with nonsmokers without passive exposure to smoking (Table 3), former smoking significantly increased breast cancer risk (OR=2.37; 95%CI=1.07-5.24). Women who smoked less than 20 years were at higher risk than those who smoked longer (OR=2.48, 95%CI=1.01-6.06). Risk for breast cancer was significantly increased in those who quit smoking at ≤ 50 years of age (OR=3.29; 95%CI=1.17-9.27) and in those who quit smoking less than 5 years before diagnosis of the disease (OR=5.46; 95%CI=1.34-22.28). In never smokers who were exposed to passive

smoking, breast cancer risk was higher than in those not exposed to passive smoking, but this difference was not significant.

Discussion

In the present study breast cancer was associated with former smoking but only in comparison with never smokers without passive exposure to smoking. Breast cancer risk was significantly increased in women who quite smoking at age ≤ 50 years, and in those who quite smoking before more than 5 years.

As already stated, data about relationship between breast cancer and smoking are inconsistent. In the year 2002, Collaborative Group on Hormonal Factors and Breast Cancer, after reanalysis of over 80% of the worldwide epidemiological data on breast cancer and tobacco consumption, concluded that smoking was not associated with breast cancer (Hamajima et al., 2002).

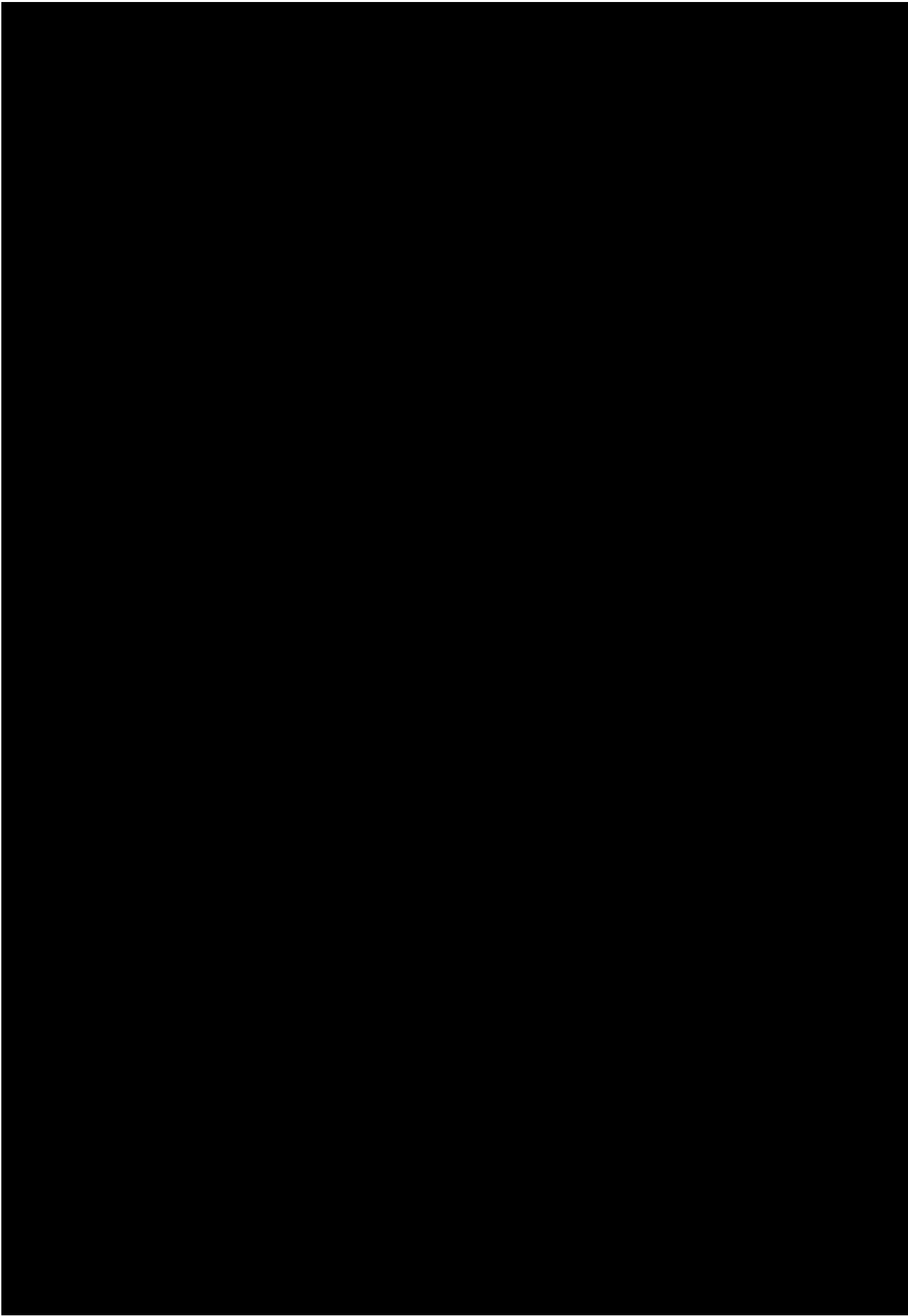
However, on the basis of the review of studies among Japanese women, Nagata et al. (2006) concluded that tobacco smoking possibly increases the risk for breast cancer. They could not explain the differences between Japanese and non-Japanese women by differences in the number of cigarettes smoked or the number of years of smoking, nor by differences in endogenous estrogen status or distribution of certain genes related to metabolic enzymes.

In the many large cohort studies reported after the year 2000 (Reynolds et al., 2004; Cui et al., 2006; Luo et al., 2011; Xue et al., 2011), although not in all of them (Lin et al., 2008; Ahern et al., 2009; Brown et al., 2010), both active and passive smoking were found to be associated with an increase in breast cancer. A Canadian Expert Panel has reviewed new studies of this subject since 2002 (Johnson et al., 2011). Based on the weight of evidence from these epidemiological and toxicological studies

Table 3. Tobacco Exposure of Cases with Breast Cancer and Their Controls

Active smoking history		Cases (N=191)		Controls (N=191)		Odds ratio (95% confidence intervals)	
		No	%	No	%	Unadjusted	Adjusted*
Passive smokers [†] excluded from reference category							
Active smoking history							
Never smokers without passive exposure		98	51.3	102	53.4	1.00 (referent)	1.00 (referent)
Never smokers with passive exposure		32	16.8	22	11.5	1.51 (0.82-2.78)	1.57 (0.81-3.03)
Ever smokers		61	31.9	67	35.1	0.95 (0.61-1.48)	1.01 (0.60-1.70)
Former smokers		25	13.1	13	6.8	2.00 (0.97-4.13)	2.37 (1.07-5.24)
Current smokers		36	18.8	54	28.3	0.69 (0.42-1.15)	0.72 (0.40-1.27)
Smoking intensity (No. of cigarettes smoked per day)	≤ 10	20	12.6	19	11.2	1.10 (0.55-2.18)	1.27 (0.60-2.71)
	11-20	31	19.5	36	21.3	0.90 (0.51-1.56)	0.94 (0.50-1.76)
	≥ 21	10	6.3	12	7.1	0.87 (0.36-2.10)	0.81 (0.31-2.17)
Total No. of smoking years	< 20	22	13.8	9	5.3	2.54 (1.12-5.79)	2.48 (1.01-6.06) [^]
	20-29	19	11.9	24	14.2	0.82 (0.42-1.69)	1.02 (0.47-2.19)
	≥ 30	20	12.6	34	20.1	0.61 (0.33-1.14)	0.65 (0.33-1.27)
Age of smoking initiation	< 20	15	9.4	23	13.6	0.68 (0.33-1.38)	0.61 (0.27-1.42)
	≥ 20	46	28.9	44	26	1.09 (0.66-1.79)	1.17 (0.67-2.05)
Years of smoking before first birth [‡]	< 5	17	14.8	18	14.6	0.97 (0.47-1.99)	1.02 (0.43-2.40)
	≥ 5	9	7.8	14	11.4	0.66 (0.27-1.60)	0.58 (0.21-1.62)
Age stopped smoking	≤ 50	18	14.6	7	6.1	2.67 (1.07-6.68)	3.29 (1.17-9.27)
	> 50	7	5.7	6	5.2	1.21 (0.39-3.74)	1.74 (0.53-7.76)
Years since quitting smoking	≤ 5	12	9.8	10	8.7	1.25 (0.52-3.02)	1.73 (0.66-4.55)
	> 5	13	10.6	3	2.6	4.51 (1.25-16.31)	5.46 (1.34-22.28)

*Multivariate model was adjusted for educational level, marital status, age at menarche, menopausal status, breastfeeding history, family history of breast cancer, body mass index, alcohol use, and cardiovascular disease in personal medical history; [†]Household and occupation passive smoking exposure; [^]After adjusting for "Years since quitting smoking", the association was not significant (OR 8.93, 95%CI 0.77-103.51); [‡]Nulliparous women were excluded from the analysis; ^{||} Only former smokers



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