BRCA2 N372H polymorphism and breast cancer risk

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INTRODUCTION

Truncating mutations in BRCA2 gene cause a substantial increase in risk of breast cancer, but such mutations are found only in small number of breast cancer patients. Low penetrance alleles, such as polymorphic variants in strongly predisposing genes, such as BRCA2, are candidates for inherited susceptibility to breast cancer. The N372H polymorphism is common variant in BRCA2 gene that was suggested to affect BRCA2 structure and function and to moderately increase the risk of breast cancer.

AIM OF THE STUDY

The aim of this study was to evaluate the possible association of this polymorphism and breast cancer risk in Macedonian patients.

MATERIALS AND METHODS

The study included 76 patients with breast cancer and 75 controls from the general population. The N372H polymorphism was screened by single strand conformation polymorphism (SSCP) method. The samples were run on 10% polyacrylamide gel. In selected samples, the results were confirmed by direct DNA sequencing on ABI 310 Genetic Analyzer (Applied Biosystems).

RESULTS

A representative photograph of N372H G->A polymorphism detection by SSCP analysis is shown in Figure 1. The allele frequency of this polymorphism in patients with breast cancer was 25.7% and was similar to the observed among controls (28.7%) (Figure2). There was no difference in the BRCA2 N372H genotype frequencies between patients with breast cancer (52.6% GG, 43.4% GA and 4.0% AA) and controls (48.0% GG, 46.7% GA and 5.3% AA) (Table1). No difference was detected when patients were classified according to the age of diagnosis and family history. In one male patient with breast cancer the N372H polymorphism was found in cis to the BRCA2 D2723H mutation.

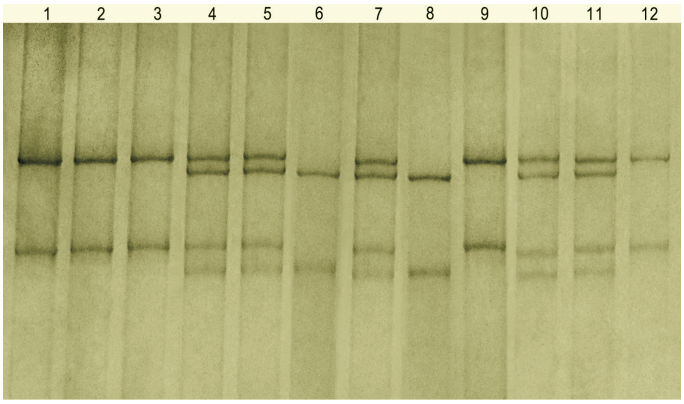

Figure 1. SSCP analysis of exon 9 of BRCA2 gene. Lines 6,8 represent N372H homozygotes (A/A), lines 4,5,7,10,11 N372H heterozygotes (G/A) and lines 1,2,3,9,12 normal controls (G/G).

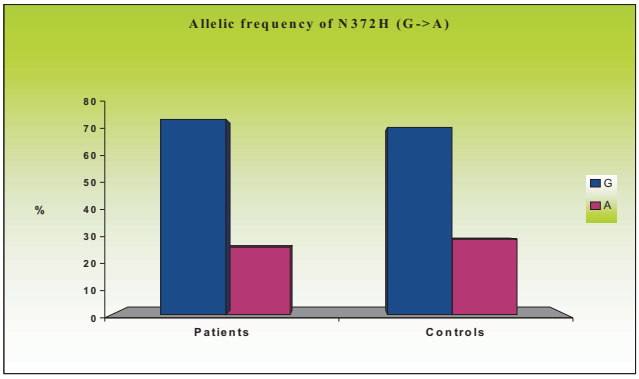

Figure 2. Distribution of N372H genotypes among breast cancer patients and normal controls.

CONCLUSIONS

In conclusion, our study has failed to support the association between N372H polymorphism and breast cancer risk.

ACKNOWLEDGMENTS

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Table 1. Genotype frequencies for N372H polymorphism among breast cancer patients and controls.

N372H Genotype	Patients (n=76)	Controls (n=75)	OR (95%CI)	p
G/G	52,63%(40)	48,00%(36)	0,63-2,28	0,5692
G/A	43,42%(33)	46,67%(35)	0,46-1.66	0,6885
A/A	3,95%(3)	5,33%(4)	0,15-3,37	0,6854