The investigation of *TP53* rs1042522 and *BBC3* rs2032809 polymorphisms and their association with early-stage breast cancer

6th Kaunas / Lithuania International
Hematology / Oncology Colloquium
28 May 2021

Justina Bekampytė[1], Agnė Bartnykaitė[1], Aistė Savukaitytė[1], Rasa Ugenskienė[1,2], Erika Korobeinikova[3], Jurgita Gudaitienė[3], Elona Juozaitytė[3]

[1]Oncology Research Laboratory, Oncology Institute, Lithuanian University of Health Sciences; [2]Department of Genetics and Molecular Medicine, Lithuanian University of Health Sciences; [3]Oncology Institute, Lithuanian University of Health Sciences

Objective

Breast cancer is one of the most common cancers among women worldwide. Apoptosis-related genes *TP53* and *BBC3* are known to play an important role in the pathogenesis of breast cancer. Studies showed that SNPs, located in genes that are involved in the regulation of apoptosis, can cause dysregulation of essential cellular processes resulting in uncontrolled cell growth. However, the roles of polymorphisms in *TP53* and *BBC3* genes have not been fully defined.

Therefore, this study aimed to analyze the association between *TP53* rs1042522 and *BBC3* rs2032809 polymorphisms and breast cancer clinicopathological features and their prognostic value in breast cancer patients.

Methods

- Lithuanian women with early-stage breast cancer were enrolled in this study (n = 171). The study group consisted of patients aged between 30 and 75 years.
- For SNP analysis genomic DNA was extracted from peripheral blood. *TP53* rs1042522 and *BBC3* rs2032809 polymorphisms were analyzed with polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) assay (Figs. 1 and 2).
- The age at the time of diagnosis, differentiation degree (G), pathological tumor size (pT), estrogen (ER) and progesterone (PR) receptors status, human epidermal growth factor receptor 2 (HER2) status, pathological lymph node status (pN), disease progression, metastasis and death were considered as clinicopathological features (Table 1). The data was collected from medical records. SPSS was used to perform statistical data analysis.
- The study was approved by Kaunas Regional Biomedical Research Ethical Committee (protocols No. BE-2-10 and No. P1-BE-2-10/2014).

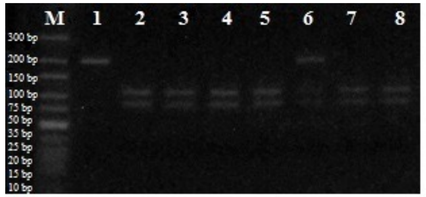

Figure 1. PCR-RFLP products of TP53 rs1042522. From left to right, lane M – DNA molecular marker GeneRuler Ultra Low Range DNA ladder (Thermo Fisher Scientific Baltics, Lithuania); lane 1 indicates CC genotype (199 bp fragment), lanes 2-5, 7-8 indicate GG genotype (113 and 86 bp fragments), lane 6 indicates CG genotype (199, 113 and 86 bp fragments).

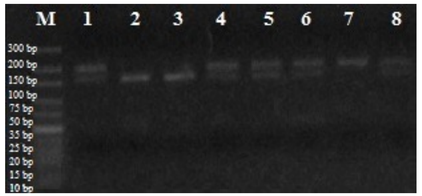

Figure 2. PCR-RFLP products of BBC3 rs2032809. From left to right, lane M – DNA molecular marker GeneRuler Ultra Low Range DNA ladder (Thermo Fisher Scientific Baltics, Lithuania); lanes 1, 4-6 and 8 indicate AG genotype (191, 157 and 34 bp fragments), lanes 2-3 indicate AA genotype (157 and 34 bp fragments), lanes 7 indicates GG genotype (191 bp fragment).

Clinicopathological features (n = 171)		%
Age at the time of diagnosis	≤ 50 years	74.9
	> 50 years	25.1
Differentiation degree (G)	G1 (well differentiated)	7.0
	G2 (moderately differentiated)	70.2
	G3 (poorly differentiated)	22.8
Pathological tumor size (pT)	T1a (0.1-0.5 cm)	71.9
	T1b (0.5-1.0 cm)	28.1
Estrogen receptor (ER)	Negative	32.2
	Positive	67.8
Progesterone receptor (PR)	Negative	40.9
	Positive	59.1
Human epidermal growth factor receptor 2 (HER2)	Negative	81.3
	Positive	18.7
Pathological lymph node (pN)	N0 (negative)	63.7
	N1 (positive)	36.3
The presence of disease progression	Absent	18.7
	Present	81.3
Development of metastasis	Absent	15.8
	Present	84.2
Patients' death	Absent	12.9
	Present	87.1

Table 1. Clinicopathological features of the patients with early-stage breast cancer

Results

- In our study *TP53* rs1042522 polymorphism did not show any statistically significant associations with clinicopathological features.
- Meanwhile, significant associations were identified between *BBC3* rs2032809 and the age at the time of diagnosis (P = 0.009), presence of disease progression (P = 0.001), development of metastasis (P = 0.003) and patients' mortality (P =0.001)
- Logistic regression showed that *BBC3* rs2032809 AG and GG genotypes were significantly associated with older age at the time of diagnosis (>50 years) (OR = 4.808, 95% CI 1.348-17.144, P = 0.015; OR = 6.552, 95% CI 1.758-24.415, P = 0.005, respectively) compared to the patients with AA genotype. Moreover, the AG genotype showed higher risk for presence of disease progression (OR = 7.892, 95% CI 2.178-28.593, P = 0.002), metastasis (OR = 5.917, 95% CI 1.622-21.593, P = 0.007) and death (OR = 17.100, 95% CI 2.178-134.257, P = 0.007) in comparison to AA genotype.
- In the survival analysis our findings revealed that patients with AG genotype of *BBC3* rs2032809 were more likely to have a shorter OS (HR = 14.523, 95% CI 1.943-108.546, P = 0.009)(Fig. 3A), PFS (HR = 7.078, 95% CI 2.130-23.521, P = 0.001)(Fig. 3B) and MFS (HR = 5.535, 95% CI 1.646-18.610, P = 0.006)(Fig. 3C) than those with AA genotype.

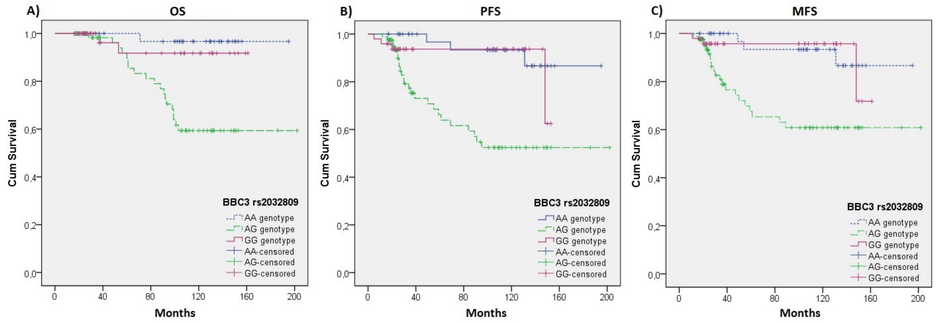

Figure 3. Kaplan-Meier curves for OS, PFS and MFS according to different BBC3 rs2032809 polymorphism genotypes

Conclusions

In conclusion, our study showed that *BBC3* rs2032809 polymorphism is associated with disease progression, development of metastasis and patient survival in early-stage breast cancer.

Key words

Breast cancer, SNPs, TP53, BBC3, associations, prognosis.