Introduction: Triple negative breast cancers (TNBC) represent 10 to 15% of all breast cancers. This subtype is characterized by the absence of the expression of estrogen receptor (ER), progesterone receptor (PR) and the absence of Her2 overexpression. TNBC has poor prognosis and does not respond to endocrine therapy or trastuzumab. The BRCA1 gene plays a key role in TNBC, where its expression can be lost in multiple ways: germinal mutation followed by deletion of the second allele, or negative regulations by promoter methylation or miRNA-mediated silencing. BRCA1-deficient tumours exhibit defect in DNA repair and respond to DNA-damaging chemotherapy or PARP inhibitors. We aimed to establish a correlation between BRCA1-related molecular parameters, other tumour characteristics and clinical follow up in order to better classify TNBC and define prognostic factors.

Method: In the tumoral tissues of 60 TNBC patients, the expression of BRCA1 protein and mRNA was quantified in situ. Promoter methylation status was established as well as cytokeratin 5 and 6 expression. Moreover, the maintenance of the interaction between BRCA1 and its interacting protein, BARD1 was tested. In parallel, the expression of 29 microRNAs reported to be correlated with survival in breast cancer was quantified.

Results: A combination of the tumoral expression of one miRNA, miR-548c and 3 other known prognostic parameters (tumour size, lymph node invasion and CK 5/6 expression status) allows relapse prediction by logistic regression with an AUC= 0.96 (95% CI, 0.883 to 1). While the 3 prognostic parameters used alone perform with an AUC = 0.75 (95% CI, 0.6 to 0.91). On the other hand, BRCA1 mRNA and protein levels, in addition to miR-210 and miR-548c tumoral expression, perform as well as the 3 known prognostic parameters (AUC = 0,82; 95% CI, 0.67 to 0.96).

Conclusion: Tumoral miR-548c expression improves the ability to predict relapse with 3 known prognostic factors in a cohort of 60 TNBC patients, highlighting miR-548c as a potential novel prognostic factor for TNBC.

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