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ORIGINAL REPORT

Imaging and histologic prognostic factors in triple-negative breast cancer and carcinoma *in situ* as a prognostic factor☆

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p53

Abstract
Objectives: To analyze what factors in magnetic resonance imaging (MRI) and histological study of triple-negative breast cancers are related to tumor recurrence and to shorter disease-free survival. To analyze survival and recurrence in function of the presence of an *in situ* component.
Material and methods: This was a retrospective study of MRI staging examinations in 122 women with triple-negative breast cancer done from 2007 through 2014. In the MRI, we evaluated morphological variables (size, margins, morphology, internal signal in T2-weighted sequences) and dynamic variables (perfusion and diffusion). In the histological study, we evaluated Ki67, p53, CK5/6, nuclear grade, and Scarff–Bloom grade, as well as the presence of an *in situ* component and tumor grade (high grade or not high grade). We compared the variables between patients with tumor recurrence and those without, and we conducted a survival analysis.
Results: Non-nodular enhancement was more common in patients with tumor recurrence ($p = 0.038$) and was associated with shorter disease-free survival ($p = 0.023$). Neither diffusion restriction ($p = 0.079$) nor Ki67 ($p = 0.052$) was associated with a worse prognosis. An *in situ* component was detected in 44% of triple-negative tumors, and a greater proportion of patients in the group with tumor recurrence had an *in situ* component; however, the presence of an *in situ* component was not associated with shorter survival ($p = 0.185$).
Conclusion: Non-nodular enhancement was associated with a worse prognosis. Diffusion restriction, Ki67, and the presence of an *in situ* component were not associated with shorter disease-free survival.

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PALABRAS CLAVE
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Ki67;
p53

Valoración de los factores pronósticos radiopatológicos del cáncer de mama triple negativo y análisis del carcinoma in situ como factor pronóstico

Resumen
Objetivos: Analizar qué factores valorados en resonancia magnética (RM) y anatomopatológicos de los tumores triple negativo (TN) se relacionan con la recidiva tumoral y con una menor supervivencia libre de enfermedad. Valorar la supervivencia y las recidivas en función de la presencia de componente *in situ* (CIS).
Material y métodos: Estudio retrospectivo de las RM realizadas desde 2007 a 2014, con inclusión de 122 mujeres con cáncer de mama TN y RM de estadificación. En RM se valoraron las características morfológicas (tamaño, márgenes, morfología y señal interna en secuencia T2) y dinámicas (perfusión y difusión). Se estudiaron también los factores anatomopatológicos (Ki67, p53, CK5/6, grado nuclear y Scarff-Bloom) y se analizó la presencia de CIS y el grado tumoral (alto o no alto grado). Se compararon las distintas variables con la presencia de recidiva y se realizó estudio de supervivencia.
Resultados: El realce no nodular presentó mayor porcentaje en el grupo de recidivas, y la diferencia fue estadísticamente significativa ($p = 0{,}038$) y se relacionó con una menor supervivencia libre de enfermedad ($p = 0{,}023$). La restricción a la difusión ($p = 0{,}079$) y el ki67 ($p = 0{,}052$) no asociaron un peor pronóstico. Se detectó CIS en el 44% de los TN, con mayor proporción en el grupo de recidiva, sin relación con una menor supervivencia ($p = 0{,}185$).
Conclusión: El realce no nodular demostró ser un factor de peor pronóstico. La restricción a la difusión, el ki67 y la presencia de CIS no se asociaron a una menor supervivencia libre de enfermedad.

Introduction

Triple negative tumors (TN) are an aggressive subgroup of breast cancer (BC) that reshows 11–20 per cent of the total. They are tumors that do not express estrogenic receptors, progesterone receptors or the receptor #2 of human epidermal growth (HER2).[1,2] They show a high mitotic index (high Ki67 expression in immunohistochemistry) and a high histologic grade (Grade 3). TN tumors are divided into four molecular subtypes: basal-*like*, apocrine molecular (better prognosis), claudin-low and the subtype associated with interferon. Basal-*like* tumors amount to 55–85 per cent of TN, they are particularly aggressive and they are defined by the expression of the epidermal growth factor receptor (EGFR) and/or cytokeratins (CK) 5/6, CK14 and CK17, by immunohistochemistry.[3] Basal-*like* tumors show mutations in the *TP53* gene and show a strong association with the suppressing role of the *BRCA1* gene – these cases have a poor prognosis.

Lack of a dominant oncogenic factor that prevents tumor proliferation limits the therapeutic options to the use of chemotherapy though they are tumors that have the best response of all to this therapy (84.6 per cent).[4]

Most TN are infiltrating ductal cancers and they are locally advanced in 23–28 per cent of the cases. In the mammography and the ultrasound they appear as lesions of benign, nodular semiology, with circumscribed edges and they do not usually associate an extensive intraductal component. The MRI is the most sensitive modality to detect these tumors. TN usually appear as unifocal lesions (66 per cent), with circumscribed edges (39 per cent), high intratumor signal in T2 sequences (necrosis), with mass-type or nodular enhancement and heterogeneous, ''ring'' internal enhancement.[5] The MRI is also the modality of choice to assess the response to primary systemic therapy (PST), since it is more objective when it comes to assessing size, tumor morphologic change (concentric, fragmented or mixed reduction), the presence of intralesion necrosis, enhancement intensity and the morphology of functional curves.

Several authors have analyzed the different radiopathological characteristics of TN tumors in an attempt to predict which are associated with a worse prognosis or a lesser response to neoadjuvant treatment. Nevertheless, there is much controversy among authors as to the association of the different MRI-assessed or anatomopathologic factors, such as the presence of carcinomas *in situ*, and their real association with a worse prognosis.

The goals of our study are:

1. To analyze what radiologic MRI-assessed and anatomopathologic factors of TN tumors are associated with tumor relapses and with a lower disease-free survival.
2. To assess disease-free survival and relapses based on the presence of *in situ* components (ISC).

Material and methods

We reviewed retrospectively all the breast MRI's performed in our center between the years 2007 and 2014 and collected a total of 122 women with TN BC. It was not necessary to obtain permission from the hospital ethics committee to conduct this study due to its retrospective nature. The