MASCC MULTINATIONAL ASSOCIATION OF SUPPORTIVE CARE IN CANCER

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Met/Met genotype correlates with increased cancer-related fatigue in breast cancer survivors

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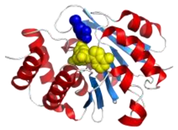
Introduction

Cancer-related fatigue (CRF) is the most common and debilitating symptom experienced by breast cancer survivors (BCS) following treatment. The influence of genetics on CRF has been sparingly investigated. In this regard, the role of the catechol-O-methyltransferase (COMT) gene in BCS is not yet fully understood. Fernández-de-las-Peñas et al. (2012) had previously revealed that genetic COMT variations could have a role in fatigue and pain reported by BCS. Furthermore, the aims of the current study are:



- To replicate the suggested impact of COMT Val158Met genotypes on fatigue in BCS after the treatment
- To explore the relevance of the Val158Met polymorphism in other related patient-reported outcomes such as quality of life, physical activity, biomarkers.

Methods

PARTICIPANTS

Inclusion criteria: 18 or older, diagnosed with localized breast cancer, finished the treatment, free from disease, and had signed the consent form.

OUTCOMES

Quality of life, health perceived, sociodemographic data, diet, and fatigue was evaluated using questionnaires.

Fatigue was assessed by the PERFORM questionnaire. It ranges from 12 to 60, with higher scores indicating lower levels of fatigue.

Physical activity, anthropometry, heart rate variability, and cardiorespiratory fitness was objectively assessed.

Blood biomarkers and clinical data were obtained by healthcare professionals from medical records. COMT genotypes. Genomic DNA of all the participants was analysed in order to study the Single Nucleotide Polymorfism rs4680 of COMT gene.

STUDY DESIGN

It is a descriptive and cross-sectional study

STATISTICAL ANALYSIS

Bivariate linear regressions were employed to assess the effects of COMT genotypes on fatigue scores. Dichotomous recodifications of COMT status were used to estimate their distinctive effect on each of the selected dependent variables. Statistical significance was determined at a p-value threshold of <0.05. All data analyses were performed utilizing STATA v 17.1

Results

- A total of 79 BCS participated
- Fatigue was related to COMT genotypes.
- Met/Met allele carriers, reported higher scores of fatigue (p=0.031).
- For the rest of the variables, no significant associations with COMT genotypes were found.

Table 1. Main descriptive data results

Variables		M (SD) or %
Age (years)		51.1 (7.7)
Time from diagnosis (years)		2.08 (1.71)
Fatigue (Perform 0-60)		47.11 (11.83)
COMT genotypes	Val/Val Met/Met Val/Met	23.5% 27.2% 49.4%

Table 2. Linear regressions results (ref. category Val/Met)

Variables	COMT	Coefficient	SE	P> t
Fatigue (PERFORM)	Val/Val	-4.93	3.47	0.161
	Met/Met	-8.057	3.64	0.031*

Conclusions

This study confirms the previously suggested association between COMT and CRF in BCS.

Future research in this field could encompass multiple polymorphisms to elucidate the mechanisms associated with fatigue in BCS.

However, we could not find any association with biomarkers. No differences were found either in cortisol levels, although in this case there was a trend towards significance (p=0.089) and could warrant further research.

Our study supports personalized medicine by identifying genetic factors that influence patient fatigue, suggesting a need for targeted interventions.

Focusing on severe fatigue groups and exploring genetic over individual determinants could improve care. Future research should include sociodemographic factors to better understand these interactions

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