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CYP17 5'-UTR *Msp*A1 polymorphism and the risk of premenopausal breast cancer in a German population-based case–control study

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Abstract

Introduction Studies on the association between the cytochrome P450c17α gene (*CYP17*) 5'-untranslated region *Msp*A1 genetic polymorphism and breast cancer risk have yielded inconsistent results. Higher levels of estrogen have been reported among young nulliparous women with the A2 allele. Therefore we assessed the impact of *CYP17* genotypes on the risk of premenopausal breast cancer, with emphasis on parity.

Methods We used data from a population-based case–control study of women aged below 51 years conducted from 1992 to 1995 in Germany. Analyses were restricted to clearly premenopausal women with complete information on *CYP17* and encompassed 527 case subjects and 904 controls, 99.5% of whom were of European descent. The *Msp*A1 polymorphism was analyzed using PCR-RFLP (PCR–restriction fragment length polymorphism) assay.

Results The frequencies of the variant allele among the cases and controls were 43% and 41%, respectively. Overall, *CYP17* A1/A2 and A2/A2 genotypes compared with the A1/A1 genotype were not associated with breast cancer, with adjusted odds ratios (ORs) of 1.04 and 1.23, respectively. Among nulliparous women, however, breast cancer risk was elevated for the A1/A2 (OR = 1.31; 95% confidence interval (CI) 0.74 to 2.32) and the A2/A2 genotype (OR = 2.12; 95% CI 1.04 to 4.32) compared with the A1/A1 genotype, with a trend towards increasing risk associated with number of A2 alleles ($P = 0.04$). Otherwise, the *CYP17* polymorphism was found neither to be an effect modifier of breast cancer risks nor to be associated with stage of disease.

Conclusion Our results do not indicate a major influence of *CYP17 Msp*A1 polymorphism on the risk of premenopausal breast cancer, but suggest that it may have an impact on breast cancer risk among nulliparous women. The finding, however, needs to be confirmed in further studies.

Introduction

The risk of breast cancer is related to genetic, environmental, and lifestyle factors that influence the level of exposure to estrogens and other sex hormones [1]. Regarding genetic factors, high-penetrance cancer-susceptibility genes such as *BRCA1* and *BRCA2* are associated with some cases of familial breast cancer, though this association accounts for only about 5% of all breast cancer cases [2], while low-penetrance genes together with endogenous and lifestyle factors are likely to account for a higher proportion of breast cancer cases [3]. These low-penetrance genes include genes involved in the metabolism of sex hormones. One such gene is *CYP17*, which codes for the enzyme cytochrome P450c17α, responsible for catalyzing steroid 17α-hydroxylase and 17,20-lyase activities at key branch points in the estrogen biosynthesis pathway [4]. An increase or decrease in activity of these enzymes may alter the level of endogenous estrogen (estradiol), thereby influencing susceptibility to breast cancer [5,6]. One of the polymorphisms of the *CYP17* gene is a thymidine substitution for cytosine (T to C) giving rise to an *Msp*A1 restriction site at nucleotide 27 in the 5'-untranslated region (5'-UTR) promoter [7]. The *Msp*A1 polymorphism has three genotypes: a

CI = confidence interval; OR = odds ratio; PCR = polymerase chain reaction; RFLP = restriction fragment length polymorphism; UTR = untranslated region.