Rs1008805 polymorphism in the CYP19A1 gene is associated with the prognosis of stage I-II and operable stage III breast cancer

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BACKGROUND: Estrogen plays a crucial role in the pathogenesis as well as the progression of breast cancer. Estrogen concentrations are 10 to 50 times higher in the malignant breast lesion than in serum, and thus, it may act locally to stimulate the growth of breast cancer. Aromatase, encoded by CYP19A1 gene, is a rate-limiting enzyme in the conversion of androgens into estrogens. It has been demonstrated that genetic polymorphisms in CYP19A1 gene were significantly correlated with altered hormone levels in urine and serum.

HYPOTHESIS: Given the critical role of CYP19A1 gene in estrogen synthesis, the potential impact of genetic polymorphisms in CYP19A1 gene on the survival of breast cancer deserves further study.

METHODS: Rs1008805 polymorphism in CYP19A1 gene were genotyped on 406 Chinese Han women with stage I-II and operable stage III breast cancer. Associations were explored between rs1008805 genotypes and disease-free survival (DFS).

RESULTS: Totally, there were 200 (49.3%) patients with AA genotype, 169 (41.6%) with AG variant, and 37 (9.1%) carrying GG variant. No significant differences were found in DFS or 5-year survival rate among the whole population with these three genotypes. However, in postmenopausal women, rs1008805 genotypes were significantly related to worse DFS and 5-years DFS rate (AA versus AG versus GG: 63.1 months versus 54.3 months versus 13.7 months; 48.6% versus 46.0% versus 14.3%; P = 0.015). In addition, women with GG variant had a poorer DFS, 5-years DFS rate when compared with those carrying AG or AA genotype (GG versus AG or AA: 13.7 months versus 56.3 months; 0% versus 52.1%; HR, 2.462; 95 % CI, 1.310-4.628; P = 0.004). Being adjusted by patients features in multivariate analyses, GG genotype remained an independent prognostic factor for DFS (HR, 2.706; 95 % CI, 1.393-5.257; P = 0.003). Besides, women with the homozygous minor allele had a marginally improved DFS, 5-years DFS rate when compared with those carrying the common allele (GG versus AG or AA: 87.0 months versus 48.7 months; 60.3% versus 42.7 %; HR, 0.544; 95% CI, 0.295-1.003; P= 0.051). However, there was no relationship between GG genotype and DFS or 5-year DFS when adjusted by patients features in multivariate analyses. The present study demonstrated that homozygous minor allele of rs1008805 SNP in CYP19A1 gene was significantly related to a worse DFS in postmenopausal women with early breast cancer. This founding is novel, if confirmed, CYP19A1 rs1008805 genotypes may turned to be a prognostic biomarker for early breast cancer.