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Association of glutathione S-transferase P1 polymorphism and endometrial cancer risk in a Chinese population.

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Abstract

The aim of this study was to investigate the relationship between glutathione S-transferase P1 (GSTP1) genetic polymorphism and endometrial cancer risk in a Chinese population. A total of 217 women diagnosed with endometrial cancer and 200 controls were retained for the present analysis. GSTP1 null genotype was significantly associated with endometrial cancer risk (OR=1.56, 95% CI 1.07-2.29, P=0.02). To further assess the effects of GSTP1 genetic polymorphism on clinical characteristics, stratification analyses were conducted. No significant association was found between GSTP1 polymorphism and BMI (OR=1.35, 95% CI 0.70-2.61, P=0.36), staging (OR=1.14, 95% CI 0.67-1.97, P=0.62) and grading (OR=0.93, 95% CI 0.52-1.57, P=0.74). In conclusion, the GSTP1 polymorphism was significantly associated with an increased risk of endometrial cancer.

Keywords: Endometrial cancer, Glutathione S-transferase P1 (GSTP1).

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Introduction

Endometrial cancer is the sixth most common cancer in women worldwide [1]. Standard treatment for localized endometrial cancer is surgery, which includes total abdominal hysterectomy with bilateral salpingo-oophorectomy [2].

Despite advances in cancer therapies, the incidence of endometrial carcinoma increases. In particular, the prognosis is poor for the patients with recurrent or advanced endometrial cancer [3].

Glutathione S-transferases (GSTs) are an important superfamily of Phase II multifunctional enzymes that contribute to the detoxification of a wide variety of natural and artificial compounds including chemotherapeutic drugs, carcinogens, and various xenobiotics [4].

Glutathione S-transferase P1 (GSTP1) regulates cellular chemical stress and death through interaction with the c-Jun Nh2-terminal kinase (JNK1) protein [5].

Bhat et al. indicated that GSTP1 shows aberrant methylation pattern in the breast cancer with the consequent loss in the protein expression [6].

Yang et al. showed that higher GSTP1 expression was shown in the Progressive Disease (PD)/Stable Disease (SD) group than in the Partial Response (PR)/Complete Response (CR) group both in the samples collected before and after the chemotherapy treatment [7].

The aim of this study was to investigate the relationship between GSTP1 genetic polymorphism and endometrial cancer risk in a Chinese population.

Methods

Study population

In the present analysis, we included 217 endometrial cancer patients and 200 controls. The 217 eligible cases were patients with endometrial cancer that was recently diagnosed and histologically confirmed during the period 2011 to 2016. The controls were also recruited from the same hospital and they were all healthy with the physical examination. The age and sex were frequency-matched between the control and case groups. Informed written consent was obtained from all participants.

DNA extraction

Firstly, 2 ml peripheral venous blood of every subject was collected in the early morning and was put into 10 mL vacuum tube with anticoagulation EDTA, stored at -80°C. Then, blood genomic DNA was extracted using TIANamp Genomic DNA Kit purchased by Tiangen Biotech (Beijing) Co., Ltd., according to the manufacturer's instruction. The isolated DNA samples were stored at -20°C refrigerator.

Genotyping

Gene polymorphism as analyzed by the Ligation Detection Reaction (LDR) method with technical support from the Biowing Applied Biotechnology (Shanghai, China). 10% of the total samples were randomly selected to repeated analyses in order to maximize the probably error of the genotyping results and improve quality control.

Statistical analysis

Statistical analyses were performed using SPSS17.0 Statistical Package (2007, SPSS Inc., Chicago, IL). Hardy-Weinberg equilibrium for genotypes was tested by goodness-of-fit χ^2 in control group. The distribution of GSTP1 genetic polymorphism was performed using the chi-square (χ^2) test to examine statistical differences between patients and controls. $P<0.05$ was considered as the significant difference.

Results

The distributions of selected characteristics among the study subjects are presented in Table 1. A total of 217 women diagnosed with endometrial cancer and 200 controls were retained for the present analysis. Median age was 67 (ranging from 51 to 81) for cases. All the patients were postmenopausal. The Body Mass Index (BMI), staging and grading were shown in Table 1.

Table 1. *Clinical characteristics of the patients.*

Characteristics	Number of patients (n=217)
Age (y)	
Median	67
Range	51-81
Postmenopausal	217
BMI (kg/m^2)	
<24.9	46
25-29.9	102
>30	69
Staging	
I	115
II	50
III	52
Grading	
G1	103
G2	85
G3	29
BMI: Body Mass Index.	

We explored the GSTP1 genetic polymorphism between the case and control groups and the results were shown in Table 2.

Table 2. *Association between endometrial cancer risk and GSTP1 polymorphism.*

Polymorphism	Case	Control	OR (95% CI)	P value
GSTP1 present	91	104	1	
GSTP1 null	126	96	1.56 (1.07-2.29)	0.02

GSTP1 null genotype was significantly associated with endometrial cancer risk (OR=1.56, 95% CI 1.07-2.29, P=0.02). To further assess the effects of GSTP1 genetic polymorphism on clinical characteristics, stratification analyses were conducted. No significant association was found between GSTP1 polymorphism and BMI (OR=1.35, 95% CI 0.70-2.61, P=0.36; Table 3), staging (OR=1.14, 95% CI 0.67-1.97, P=0.62), and grading (OR=0.93, 95% CI 0.52-1.57, P=0.74).

Table 3. *Association between clinical characteristics and GSTP1 polymorphism.*

Characteristics	GSTP1 present	GSTP1 null	OR (95% CI)	P value
BMI (kg/m^2)				
<24.9	22	24	1	
>25	69	102	1.35 (0.70-2.61)	0.36
Staging				
I	50	65	1	
II+III	41	61	1.14 (0.67-1.97)	0.62
Grading				
G1	42	61	1	
G2+G3	49	65	0.93 (0.52-1.57)	0.74
BMI: Body Mass Index.				

Discussion

In the current study, we demonstrated that there was a significant association between GSTP1 polymorphism and endometrial cancer risk. However, no significant association was found between GSTP1 polymorphism and BMI, staging, and grading.

Gao et al. suggested that GSTP1 rs1695 and GPX1 rs1050450 SNPs have no effects on the risk of preeclampsia in the Chinese Han population [8]. Zhang et al. indicated that GSTP1 Ile105Val polymorphism was associated with urinary system cancer susceptibility [9]. Hassani et al. showed that GSTM1 and GSTP1 polymorphisms may be associated with susceptibility of endometriosis in Iranian women [10]. Nasr et al. demonstrated that GSTM1 null or GSTT1 null genotypes may be considered independent risk factors for acute myeloid leukemia [11]. Qi et al. suggested that GSTP1 Val/Val genotypes may contribute to genetic susceptibility to ARC in Chinese Han Population [12]. However, Zhao et al. showed that GSTP1 Ile105Val polymorphisms might not be significantly associated with coronary heart disease risk [13].

We acknowledge that there are several limitations in the current study. First, restrained by the moderate sample size and lack of a validation cohort. Second, case-control studies tend to be susceptible to selection bias, particularly in the control

group. Third, we did not asses jointly the influence of genetic characteristics of the host factors.

Conclusion

The GSTP1 polymorphism was significantly associated with an increased risk of endometrial cancer. Future studies involving larger control and case populations are warranted in order to corroborate the association.

Conflicts of Interest

None.

References

1. Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, Ledermann J, Marth C, Nout R, Querleu D, Mirza MR, Sessa C. ESMO-ESGO-ESTRO Endometrial Consensus Conference Working Group. ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: Diagnosis, Treatment and Follow-up. Int J Gynecol Cancer 2016; 26: 2-30.
2. Fader AN, Arriba LN, Frasure HE, von Gruenigen VE. Endometrial cancer and obesity: epidemiology, biomarkers, prevention and survivorship. Gynecol Oncol 2009; 114: 121-127.
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin 2015; 65: 5-29.
4. Hayes JD, Pulford DJ. The glutathione S-transferase supergene family: regulation of GST and the contribution of the isoenzymes to cancer chemoprotection and drug resistance. Crit Rev Biochem Mol Biol 1995; 30: 445-600.
5. Adler V, Yin Z, Fuchs SY, Benezra M, Rosario L, Tew KD, Pincus MR, Sardana M, Henderson CJ, Wolf CR, Davis RJ, Ronai Z. Regulation of JNK signaling by GSTp. Embo J 1999; 18: 1321-1334.
6. Bhat A, Masood A, Wani KA, Bhat YA, Nissar B, Khan NS, Ganai BA. Promoter methylation and gene polymorphism are two independent events in regulation of GSTP1 gene expression. Tumour Biol 2017; 39: 1010428317697563.
7. Yang SJ, Wang DD, Li J, Xu HZ, Shen HY, Chen X, Zhou SY, Zhong SL, Zhao JH, Tang JH. Predictive role of GSTP1-containing exosomes in chemotherapy-resistant breast cancer. Gene 2017; 623: 5-14.
8. Gao H, Liu C, Lin P, Xu L, Li X, Chen Y, Cheng B, Li A, Liu S. Effects of GSTP1 and GPX1 Polymorphisms on the risk of preeclampsia in chinese han women. Cell Physiol Biochem 2016; 39: 2025-2032.
9. Zhang Y, Yuan Y, Chen Y, Wang Z, Li F, Zhao Q. Association between GSTP1 Ile105Val polymorphism and urinary system cancer risk: evidence from 51 studies. Onco Targets Ther 2016; 9: 3565-3569.
10. Hassani M, Saliminejad K, Heidarizadeh M, Kamali K, Memariani T, Khorram Khorshid HR. Association study of glutathione s-transferase polymorphisms and risk of endometriosis in an Iranian population. Int J Reprod Biomed (Yazd) 2016; 14: 241-246.
11. Nasr AS, Sami RM, Ibrahim NY, Darwish DO. Glutathione S transferase (GSTP 1, GSTM 1 and GSTT 1) gene polymorphisms in Egyptian patients with acute myeloid leukemia. Indian J Cancer 2015; 52: 490-495.
12. Qi R, Gu Z, Zhou L. The effect of GSTT1, GSTM1 and GSTP1 gene polymorphisms on the susceptibility of age-related cataract in Chinese Han population. Int J Clin Exp Med 2015; 8: 19448-19453.
13. Zhao E, Zhao Y. Lack of association between GSTP1 Ile105Val polymorphism and coronary heart disease risk: a meta-analysis. Int J Clin Exp Med 2015; 8: 18488-18493.

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