

## **Glutathione S-transferase M1 polymorphism and the risk of pancreatitis.**

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### **Abstract**

Previous meta-analysis has found that no significant relationship between GSTM1 and chronic pancreatitis risk. However, we found a mistake in the abstract of the data in that meta-analysis. Additionally, new study was published. Thus, we conducted this meta-analysis. We did a systematic search of PubMed, EMBASE, Web of Science, and CNKI up to May 2017. We included 8 studies with 751 cases and 1614 controls in this meta-analysis. Subjects with GSTM1 null genotype were significantly associated with an increased risk for pancreatitis compared those carrying the GSTM1 present genotype (OR=1.17, 95% CI: 1.05-1.30). In addition, GSTM1 null genotype was significantly associated with chronic pancreatitis risk (OR=1.17, 95% CI: 1.05-1.30). Furthermore, Caucasians with GSTM1 null genotype showed an increased pancreatitis risk (OR=1.19, 95% CI: 1.06-1.32). In conclusion, this study indicated that GSTM1 null genotype were significantly associated with an increased risk for pancreatitis.

**Keywords:** GSTM1, Pancreatitis, Polymorphism.

*Accepted on July 26, 2017*

### **Introduction**

Pancreatitis is a pancreas inflammatory disorder. It has high mortality and significant global socioeconomic burden [1]. Chronic pancreatitis carries a high burden of morbidity because of its long duration and recurrent attacks. Acute pancreatitis is an inflammatory condition of the pancreas with a clinical course that varies from mild to severe.

The superfamily of Glutathione S transferases (GSTs) is associated with the regulation of inflammation through modulation of prostaglandin signaling pathways and oxidative stress and through the regulation of normal cellular physiology [2,3]. The GSTM1 locus has been mapped on chromosome 1p13.3. Persons with deletion of the GSTM1 locus have no enzymatic functional activity of the enzyme [4]. Hu et al. found that the GSTM1 null genotype might be significantly associated with a reduced overall survival in breast cancer [5]. Huang et al. found that GSTM1 and GSTT1 polymorphisms contribute to renal cell carcinoma risk by a meta-analysis [6]. Lu et al. suggested that GSTM1 null polymorphism may be associated with an increased risk for esophageal cancer in Asian [7]. Sun et al. suggested that GSTM1 null genotype may contribute to the cervical cancer development in Chinese [8]. A meta-analysis has found that no significant relationship

between GSTM1 and chronic pancreatitis risk [9]. However, we found a mistake in the abstract of the data in that meta-analysis. Additionally, new study was published [10]. Thus, we conducted this meta-analysis to investigate the association between GSTM1 null polymorphism and pancreatitis risk.

### **Materials and Methods**

#### ***Publications search***

We did a systematic search of PubMed, EMBASE, Web of Science, and CNKI up to May 2017 by using the combination of the following key words: “glutathione S-transferase M1”, “GSTM1”, “polymorphism”, and “pancreatitis”. Additional eligible studies were identified through references that were cited in the relevant articles.

#### ***Inclusion criteria***

All selected studies complied with the following criteria: (1) The study design should be case-control study; (2) The study should investigate the association between GSTM1 null polymorphism and pancreatitis risk; and (3) The study should have genotype frequencies of cases and controls.

**Data extraction**

Two of the authors extracted all data independently following the selection criteria. The following data were collected from each study: the first author, year, ethnicity, age, gender, sample size, and subtype of pancreatitis.

**Statistical analysis**

Crude Odds Ratios (ORs) and 95% Confidence Intervals (CIs) were used to estimate the strength of the relationship between the GSTM1 null polymorphism and pancreatitis risk. The heterogeneity was estimated using the  $\chi^2$ -based Q statistic, and heterogeneity was considered statistically significant when P heterogeneity  $\leq$  0.1. The statistical analyses were performed using Review Manager Software (v.5.0; Oxford, England) with two-sided P values and a 0.05 significance level.

**Results**

**Characteristics of the studies**

We included 8 studies with 751 cases and 1614 controls in this meta-analysis [10-17]. Seven of the studies were conducted in Caucasians, and one study was conducted in Asians, respectively. Seven studies included chronic pancreatitis

**Table 1.** Characteristics of included studies [10-17].

First author	Ethnicity	Age	Gender	Type of pancreatitis	Case (n)	Control (n)
Bartsch [11]	Caucasian	NA	Mixed	Chronic pancreatitis	114	78
Frenzer [12]	Caucasian	53	Mixed	Chronic pancreatitis	71	257
Verlaan [13]	Caucasian	NA	Mixed	Chronic pancreatitis	142	261
Burim [14]	Caucasian	NA	NA	Chronic pancreatitis	14	262
Schneider [15]	Caucasian	NA	NA	Chronic pancreatitis	103	183
Rahman [16]	Caucasian	51	Mixed	Chronic pancreatitis	121	245
Maruyam [17]	Asian	59	NA	Chronic pancreatitis	53	96
Martins [10]	Caucasian	NA	Mixed	Acute pancreatitis	133	232

NA: Not Available.

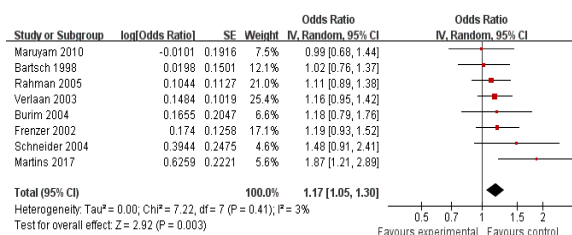
**Table 2.** Summary of results from meta-analysis and subgroup analysis.

	No. of studies	OR (95% CI)	P value	P heterogeneity
Pancreatitis	8	1.17 (1.05-1.30)	0.003	0.41
Chronic pancreatitis	7	1.14 (1.02-1.26)	0.02	0.87
Caucasian	7	1.19 (1.06-1.32)	0.003	0.38

patients and one study included acute pancreatitis patients. The main characteristics of these studies are presented in Table 1.

**Meta-analysis**

The random-effects model (DerSimonian-Laird method) was used to calculate the pooled ORs. Subjects with GSTM1 null genotype were significantly associated with an increased risk for pancreatitis compared those carrying the GSTM1 present genotype (OR=1.17, 95% CI: 1.05-1.30, Figure 1). In addition, GSTM1 null genotype was significantly associated with chronic pancreatitis risk (OR=1.17, 95% CI: 1.05-1.30, Table 2). Furthermore, Caucasians with GSTM1 null genotype showed an increased pancreatitis risk (OR=1.19, 95% CI: 1.06-1.32, Table 2).



**Figure 1.** The association between GSTM1 null genotype and the risk for pancreatitis.

**Discussion**

In this update meta-analysis, we included 8 studies with 751 cases and 1614 controls. Subjects with GSTM1 null genotype were significantly associated with an increased risk for pancreatitis compared those carrying the GSTM1 present genotype. In addition, GSTM1 null genotype was significantly associated with chronic pancreatitis risk. Furthermore, Caucasians with GSTM1 null genotype showed an increased pancreatitis risk.

Cho et al. found that variants of PRSS1, SPINK1, and CFTR were associated with idiopathic pancreatitis [18]. Gui et al. suggested that the IL-18-607C/A and -137G/C polymorphisms do not influence susceptibility to acute pancreatitis in the Chinese population [19]. Padureanu et al. found that the risk of developing chronic pancreatitis was not increased by the presence of the iNOS-2087A>G polymorphism [20]. Anilir et al. indicated that IL-8 AA genotype was detected with a significantly higher frequency among the patients with acute biliary pancreatitis [21]. Ma et al. found that *LP-PLA2* gene polymorphisms, V279F and R92H, may be associated with susceptibility to and severity of acute pancreatitis [22].

The present study does have limitations. Firstly, we failed to make the subgroup analysis stratified by different genetic backgrounds because of insufficient data. Second, gene-gene or gene-environment interactions were not incorporated in this study. Third, only one study with Asians was included.

In conclusion, this study indicated that GSTM1 null genotype were significantly associated with an increased risk for pancreatitis.

### Disclosure of Conflict of Interest

The authors have declared that no competing interests exist.

### Acknowledgment

This study was supported by National Natural Science Foundation of China (No. 81260087 and 81560111).

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