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

Minzhen Qin¹, Mengbin Qin², Zhihai Liang³, Guodu Tang³*

¹Department of Clinical Medicine, the First Clinical Medical School of Guangxi Medical University, Nanning, Guangxi, PR China
²Department of Gastroenterology, the Second Affiliated Hospital of Guangxi Medical University, Nanning, Guangxi, PR China
³Department of Gastroenterology, the First Affiliated Hospital of Guangxi Medical University, Nanning, Guangxi, PR China

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.

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

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

<table>
<thead>
<tr>
<th>First author</th>
<th>Ethnicity</th>
<th>Age</th>
<th>Gender</th>
<th>Type of pancreatitis</th>
<th>Case (n)</th>
<th>Control (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frenzer [12]</td>
<td>Caucasian</td>
<td>53</td>
<td>Mixed</td>
<td>Chronic pancreatitis</td>
<td>71</td>
<td>257</td>
</tr>
<tr>
<td>Verlaan [13]</td>
<td>Caucasian</td>
<td>NA</td>
<td>Mixed</td>
<td>Chronic pancreatitis</td>
<td>142</td>
<td>261</td>
</tr>
<tr>
<td>Burim [14]</td>
<td>Caucasian</td>
<td>NA</td>
<td>NA</td>
<td>Chronic pancreatitis</td>
<td>14</td>
<td>262</td>
</tr>
<tr>
<td>Schneider [15]</td>
<td>Caucasian</td>
<td>NA</td>
<td>NA</td>
<td>Chronic pancreatitis</td>
<td>103</td>
<td>183</td>
</tr>
<tr>
<td>Rahman [16]</td>
<td>Caucasian</td>
<td>51</td>
<td>Mixed</td>
<td>Chronic pancreatitis</td>
<td>121</td>
<td>245</td>
</tr>
<tr>
<td>Maruyam [17]</td>
<td>Asian</td>
<td>59</td>
<td>NA</td>
<td>Chronic pancreatitis</td>
<td>53</td>
<td>96</td>
</tr>
</tbody>
</table>

NA: Not Available.

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 (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).

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

Table 2. Summary of results from meta-analysis and subgroup analysis.
Glutathione S-transferase M1 polymorphism and the risk of pancreatitis

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).

References


*Correspondence to
Guodu Tang
Department of Gastroenterology
The First Affiliated Hospital of Guangxi Medical University
PR China