RESEARCH ARTICLE

Association of the Glutathione S-transferase T1 Null Genotype with Risk of Gastric Cancer: a Meta-analysis in Asian Populations

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Abstract

Background: A large number of studies have been published to investigate the association between the null genotype of glutathione S-transferase T1 (*GSTT1*) with gastric cancer. However, the results were inconsistent and conflicting. The aim of this study was to estimate the relationship between this polymorphism in the *GSTT1* gene and gastric cancer risk in Asian populations by meta-analysis. Materials and Methods: A literature search was performed in PubMed, Embase, Chinese Biomedical database (CBM), Weipu database, Wanfang database, and China National Knowledge Infrastructure database (CNKI). Statistical analysis was conducted by using Review Manager 5.3. Results: Thirty-nine studies with a total of 7,737 gastric cancer cases and 10,823 controls were included in this meta-analysis. The meta-analysis of total studies showed that the null genotype in *GSTT1* was associated with increased risk of gastric cancer in Asians (OR=1.19, 95% CI=1.08-1.31, *p*=0.0002). Subgroup analysis showed a significant relationship between *GSTT1* null genotype and gastric cancer in East-Asians, as well as in subgroup analysis of hospital-based design. On subgroup analysis by smoking status, alcohol status, *Helicobacter pylori* infection status, and histology type, no significant association of this polymorphism with susceptibility to gastric cancer was found. Conclusions: In conclusion, the results showed that the null genotype of *GSTT1* is significantly associated with an increased risk in gastric cancer in Asian populations.

Keywords: *GSTT1* - polymorphism - gastric cancer - meta-analysis - Asia

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Introduction

It is estimated that by 2020, more than 15 million cases of cancer will occur in the world, with deaths increasing to 12 million (Kanavos, 2006). According to the report, gastric cancer is the fourth most common malignancy among worldwide and the second leading cause of global cancer death, which has a high incidence in Asia, especially in Eastern Asia (Jemal et al., 2011). Identifying risk factors for gastric cancer development is essential to prevent this deadly disease. Numbers of studies have been shown that gastric cancer is a disease of multiple etiologic factors involving infectious, nutritional and environmental factors (Setiawan et al., 2000; Tripathi et al., 2011; Shi et al., 2014). However, the regional differences in the incidence of gastric cancer worldwide might imply that variants in various genetic factors also influence the susceptibility to this disease (Jing et al., 2012).

Human glutathione S-transferases T1 (*GSTT1*) is phase II metabolizing enzyme protecting against cancer by detoxifying numerous potentially cytotoxic/genotoxic compounds, which has been implicated in the carcinogenic process in many cancers, such as lung cancer, laryngeal cancer and esophageal cancer (Acar et al., 2006; Sreeja et al., 2008; Liu et al., 2010). Polymorphisms in this gene affect the enzymatic activities and the ability to metabolize carcinogenic compounds (Nebert et al., 1999). The most common variant of *GSTT1* gene is homozygous deletion (null genotype), which has been reported to be associated with gastric cancer (Hayes and Strange, 2000). However, the sparseness of data or disagreements among the reported investigations results in the available evidence weakly. To assess the effect of *GSTT1* null genotype on gastric cancer risk in Asian population more precisely, we conducted most of the related studies and performed this meta-analysis of published data investigating whether the null genotype of *GSTT1* gene was associated with the risk of gastric cancer.

Materials and Methods

Publication search

A literature search of PubMed, Embase, Chinese Biomedical database (CBM), Weipu database, Wanfang

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database and Chinese National Knowledge Infrastructure (CNKI) was conducted using combinations of the following keywords: "gastric cancer or gastric carcinoma or gastric neoplasm" and "polymorphism or variant or mutation" and "*GSTT1* or glutathione S-transferase T1". The language was limited to Chinese and English. All studies that evaluate the relationship between polymorphisms in *GSTT1* gene and gastric cancer risk were retrieved. Studies included in the meta-analysis had to meet all of the following criteria: (1) evaluation of the polymorphisms in *GSTT1* gene and gastric cancer risk, (2) use of a case-control design, (3) published in a journal, (4) sufficient genotype data for estimating the odds ratio (OR) with 95% confidence intervals (CI). The exclusion criteria were: (1) abstracts and reviews, (2) studies that did not offer genotype frequency. Additionally, in studies with overlapping or repeating data, the most recent or complete studies with the largest sample size were recruited into the meta-analysis.

Data extraction

Two of the authors extracted all data independently (YZ and LCD), complied with the selection criteria, and must reach a consensus on all items. In case of conflicting evaluations, a third author (JB) assessed the articles. The following information were collected: first author's name, year of publication, country of origin, cancer type, genotyping method, mean age of case, total number of cases and controls, and genotype distributions (both null *GSTT1* and non-null *GSTT1*) in cases and controls. The distributions of *GSTT1* genotypes in subgroups (smoking status, alcohol status, Helicobacter pylori (*H. pylori*) infection status, and histology type) were also elicited.

Statistical analysis

Statistical analysis was conducted by using Review Manager 5.3 and STATA 12.0. The strength of association between *GSTT1* null polymorphism and gastric cancer risk was assessed as OR with corresponding 95% CI. The significance of the pooled OR was evaluated by using a Z-test and $p<0.05$ was considered statistically significant.

Heterogeneity among studies was valued by Chi-square test, which was considered significant for $p\leq0.10$. The fixed-effects and random-effects model were used to pool the results, when $p\leq0.10$, a random-effects model was used; when $p>0.10$, a fixed-effects model was utilized. Six subgroups were analyzed to evaluate subregion-specific, study design-specific, smoking status-specific, alcohol status-specific, *H. pylori* infection status-specific and histology type-specific effects, which were performed by subregion group (East-Asia, South-Asia, Southeast-Asia and West-Asia), study design (Hospital-based study and Population-based study), smoking status (Smoking and Non-smoking), alcohol status (Alcohol and Non-alcohol), *H. pylori* infection status (Infection and Non-infection), and histology type (Diffuse and Intestinal). Sensitivity analysis was conducted by sequentially excluding each study to check the stability of the result. Inverted funnel plots was utilized to provide a diagnosis of publication bias and the degree of asymmetry was tested by Egger's test ($p<0.05$ was considered significant).

Results

Study selection and study characteristics

As shown in Figure 1, a total of 214 results relevant to the search terms in the selected databases were identified. In the first selection, 114 were included to more careful screening, 100 were excluded for not involving polymorphisms in *GSTT1* gene and risk of gastric cancer. After reading the titles and abstracts, 52 articles were included for full-text view, 62 articles were excluded for not investigating the association between *GSTT1* and gastric cancer in Asians. 13 articles were excluded after reading the full text. Six were not Asians studies (Gonzalez et al., 2004; Martinez et al., 2006; Ruzzo et al., 2007; Wideroff et al., 2007; Zendehdel et al., 2009; Garcia-Gonzalez et al., 2012), and seven were repeating or overlapping publications (Cai et al., 1999; Setiawan et al., 2001; Gao et al., 2002b; Qian et al., 2003; Sheng et al., 2004; Nan et al., 2005b; Tripathi et al., 2008). Finally, 39 articles that report on the effects of *GSTT1* polymorphisms on gastric cancer in Asia covering in total of 7,737 gastric cancer cases and 10,823 controls were remained for data extraction. 11 of them were Chinese (Qian et al., 2001; Sheng and Wang, 2002; Zheng et al., 2002; Liu et al., 2003; Ye et al., 2003; Zhang et al., 2003; Zhou et al., 2003; Xie et al., 2008; Feng et al., 2010; Liu et al., 2013; Shi et al., 2014), and 28 were English (Katoh et al., 1996; Setiawan et al., 2000; Cai et al., 2001; Saadat and Saadat, 2001; Gao et al., 2002a; Wu et al., 2002; Choi et al., 2003; Roth et al., 2004; Mu et al., 2005; Nan et al., 2005a; Sheng et al., 2005; Tamer et al., 2005; Hong et al., 2006; Al-Moundhri et al., 2009; Malik et al., 2009; Masoudi et al., 2009; Moy et al., 2009; Piao et al., 2009; Nguyen et al., 2010; Yadav et al., 2010; Luo et al., 2011; Tripathi et al., 2011; Yadav et al., 2011; Zhang et al., 2011; Jing et al., 2012; Malakar et al., 2012; Eom et al., 2013; Haholu et al., 2013). The characteristics of included studies were summarized in Table 1. The distribution of *GSTT1* genotypes in the subgroups were shown in Table 2.

Meta-analysis results

The heterogeneity was analyzed for all 39 studies and the value of Chi-square test was 65.85 with 38 degrees of freedom and $p=0.003$ in a random-effects model. Overall,

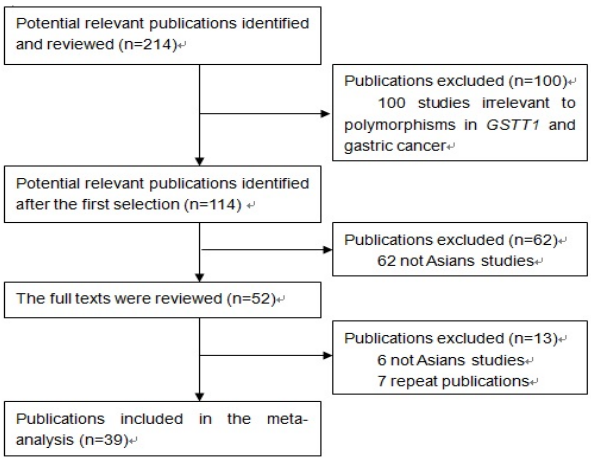

Figure 1. Flow Biagram for Selection of Studies

Table 1. Characteristics of Case-Control Studies in the Meta-Analysis

Study	Country	Subregion	Cancer type	Study design	Sample size (case/control)	Genotype frequency of GSTT1				Case age (year)	Genotyping method
						Case		Control			
						Null	Non-Null	Null	Non-Null		
Al-Moundhri 2009	Oman	West-Asia	GC	PB	107/107	19	88	20	87	NA	Multiplex-PCR
Cai 2001	China	East-Asia	GC	PB	95/94	41	54	47	47	59	PCR
Choi 2003	Korea	East-Asia	GAC	HB	80/177	43	37	94	83	NA	PCR
Eom 2013	Korea	East-Asia	GC	HB	477/477	210	267	211	265	57.8	Multiplex-PCR
Feng 2010	China	East-Asia	GC	HB	585/585	259	326	247	338	61.7	PCR
Gao 2002	China	East-Asia	GC	PB	153/223	71	82	119	104	60.8	Multiplex-PCR
Haholu 2013	Turkey	West-Asia	GC	HB	50/57	10	40	16	41	NA	Duplex-PCR
Hong 2006	Korea	East-Asia	GAC	PB	108/238	45	63	119	119	62	Multiplex-PCR
Jing 2012	China	East-Asia	GC	HB	410/410	236	174	202	208	49.5	PCR-CTPP
Katoh 1996	Japan	East-Asia	GAC	PB	139/126	66	73	56	70	62	Multiplex-PCR
Liu 2003	China	East-Asia	GAC	HB	127/114	76	51	55	59	55	Multiplex-PCR
Liu 2013	China	East-Asia	GC	PB	110/220	49	61	73	147	56.2	PCR
Luo 2011	China	East-Asia	GC	PB	123/129	77	46	63	66	55.2	PCR-RFLP
Malakar 2012	India	South-Asia	GC	PB	102/204	37	65	93	111	NA	PCR
Malik 2009	India	South-Asia	GC	PB	108/195	33	75	49	146	55.9	Multiplex-PCR
Masoudi 2009	Iran	West-Asia	GC	HB	92/134	50	42	38	96	57.7	PCR
Moy 2009	China	East-Asia	GC	PB	170/735	97	73	415	320	58.2	TaqMan-PCR
Mu 2005	China	East-Asia	GC	PB	196/393	93	103	192	201	NA	PCR-RFLP
Nan 2005	Korea	East-Asia	GC	HB	400/614	171	229	247	367	60	Multiplex-PCR
Nguyen 2010	Vietnam	Southeast-Asia	GC	HB	59/100	25	34	38	62	62.8	Multilex-PCR
Piao 2009	Korea	East-Asia	GC	PB	2212/1699	1172	1041	858	841	60.2	TaqMan-PCR
Qian 2001	China	East-Asia	GC	PB	89/94	51	38	46	48	62	PCR
Roth 2004	China	East-Asia	GC	PB	90/454	43	47	243	211	60.4	TaqMan-PCR
Saadat 2001	Iran	West-Asia	GC	NA	42/131	15	27	41	90	NA	PCR
Setiawan 2000	China	East-Asia	GAC	PB	73/417	44	37	190	228	NA	PCR-RFLP
Sheng 2002	China	East-Asia	GC	PB	110/675	43	67	309	366	59.3	PCR-RFLP
Sheng 2005	China	East-Asia	GAC	PB	121/121	64	57	54	67	59.7	PCR
Shi 2014	China	East-Asia	GC	PB	60/83	34	26	33	50	55.6	Multiplex-PCR
Tamer 2005	Turkey	West-Asia	GC	PB	70/204	21	49	53	151	57.7	Real-time PCR
Tripathi 2011	India	South-Asia	GC	NA	82/89	29	53	19	70	54.3	PCR
Wu 2002	China	East-Asia	GAC	HB	356/278	181	175	130	148	62	Multiplex-PCR
Xie 2008	China	East-Asia	GAC	HB	70/100	48	22	50	50	56.6	PCR
Yadav 2010	India	South-Asia	GAC	PB	133/270	50	83	85	185	NA	Multiplex-PCR
Yadav 2011	India	South-Asia	GC	PB	41/130	6	35	14	116	51.9	Multiplex-PCR
Ye 2003	China	East-Asia	GAC	HB	56/56	34	22	26	30	57.6	Multiplex-PCR
Zhang 2003	China	East-Asia	GAC	HB	127/114	76	51	55	59	55	Multiplex-PCR
Zhang 2011	China	East-Asia	GC	HB	194/412	114	80	198	214	46.4	PCR
Zheng 2002	China	East-Asia	GC	PB	92/92	49	43	38	54	53.2	PCR
Zhou 2003	China	East-Asia	GAC	HB	19/72	10	9	28	44	54.5	Multiplex-PCR

GC, gastric cancer; GAC, gastric adenocarcinoma; HB, hospital-based study; PB, population-based study; NA, not available; PCR, polymerase chain reaction; RFLP-PCR, polymerase chain reaction-restriction fragment length polymorphism; Multiplex-PCR, multiplex polymerase chain reaction; Null, null genotype in GSTT1; Non-null, non-null genotype in GSTT1

there was statistical evidence of an association between the null genotype of *GSTT1* and gastric cancer risk. OR was 1.19 (95% CI=1.08-1.31) and the test for overall effect Z value was 3.68 (p=0.0002). The results suggested that null genotype in *GSTT1* have an increased risk of gastric cancer (Figure 2).

In subgroup analysis by subregion, there was a significant association between *GSTT1* null genotype and gastric cancer in East-Asia population (OR=1.16, 95% CI=1.06-1.27, p=0.002), but no significant association was found in South-Asia population (OR=1.21, 95% CI=0.84-1.75, p=0.3), Southeast-Asia population (OR=1.20, 95% CI=0.62-2.31, p=0.59) and West-Asia population (OR=1.28, 95% CI=0.76-2.16, p=0.35) (Figure 3). In

Table 2. The Frequency Distributions of the GSTT1 Genotypes in the Subgroups

	Study	Yes				No			
		Case		Control		Case		Control	
		null	non-null	null	non-null	null	non-null	null	non-null
Smoking[a]	Gao 2002	61	62	67	60	10	20	52	44
	Hong 2006	26	34	54	50	19	29	64	70
	Malakar 2012	27	54	56	74	10	11	37	45
	Setiawan 2000	23	19	63	82	21	18	127	146
	Shi 2014	29	10	11	18	5	16	22	32
	Tamer 2005	10	24	18	66	11	25	35	85
Alcohol[b]	Gao 2002	28	29	25	28	43	53	94	76
	Hong 2006	15	27	52	40	30	36	68	78
	Setiawan 2000	14	13	65	70	30	24	125	158
H. pylori[c] *infection*	Hong 2006	29	42	61	69	15	22	57	51
	Setiawan 2000	25	21	121	128	14	9	59	85
	Tripathi 2011	21	30	14	51	8	23	5	19
Histology[d]	Choi 2003	12	16	94	83	31	21	94	83
	Hong 2006	19	31	119	119	15	20	119	119
	Liu 2003	28	23	55	59	48	28	55	59
	Zhang 2003	28	23	55	59	48	38	55	59

[a]Yes, smoking status; No, no-smoking status; [b]Yes, alcohol status; No, no-alcohol status; [c]Yes, infection status; No, no-infection status; [d]Yes, diffuse histology; No, intestinal histology.

Table 3. The Results of Pooled Odds Ratio (OR) with 95 % Confidence Interval (CI) in the Meta-analysis

	N	Sample size	Analysis model	Test of association		Test for heterogeneity
		(case/control)		OR (95% CI)	p^a	p^b
Total	39	7737/10823	R	*1.19 [1.08, 1.31]*	0.0002	0.003
Subregion						
East-Asia	28	6851/9202	R	*1.16 [1.06, 1.27]*	0.002	0.02
South-Asia	5	466/888	R	1.21 [0.84, 1.75]	0.3	0.1
Southeast-Asia	1	59/100	R	1.20 [0.62, 2.31]	0.59	NA
West-Asia	5	361/633	R	1.28 [0.76, 2.16]	0.35	0.02
Study design						
PB	22	4511/6904	R	1.09 [0.97, 1.23]	0.16	0.05
HB	15	3226/3919	R	*1.32 [1.14, 1.52]*	0.0003	0.03
Smoking status						
Smoking	6	379/619	R	1.03 [0.79, 1.34]	0.83	0.01
Non-smoking	6	195/759	F	0.83 [0.60, 1.15]	0.25	0.28
Alcohol status						
Alcohol	3	126/280	F	0.79 [0.51, 1.23]	0.3	0.13
Non-alcohol	3	216/599	F	0.95 [0.70, 1.31]	0.77	0.08
H. pylori infection						
Infection	3	168/444	R	1.29 [0.68, 2.44]	0.43	0.07
Non-infection	3	91/276	R	1.17 [0.50, 2.75]	0.72	0.09
Histology type						
Diffuse	4	180/643	F	0.92 [0.66, 1.29]	0.64	0.22
Intestinal	4	249/643	F	1.30 [0.96, 1.77]	0.09	0.31

Bold values are statistically significant; N, number of studies; OR, odds ratio; CI, confidence interval; F, fixed-effect model; R, random-effect model; *H. pylori*, Helicobacter pylori; NA, not applicable; [a]*p*, value for Z-test; [b]*p*, value for Chi-square test

subgroup analysis of study design, for population-based study (OR=1.09, 95% CI=0.97-1.23, *p*=0.16), for hospital-based study (OR=1.32, 95% CI=1.14-1.52, *p*=0.0003) (Figure 4). Additionally, no significant associations were found between *GSTT1* null genotype and gastric cancer both in the subgroup analysis of smoking status (Smoking, OR=1.03, 95% CI=0.79-1.34, *p*=0.83; Non-smoking, OR=0.83, 95% CI=0.60-1.15, *p*=0.25), alcohol status (Alcohol, OR=0.79, 95% CI=0.51-1.23, *p*=0.3; Non-alcohol, OR=0.95, 95% CI=0.7-1.13, *p*=0.77), *H. pylori*

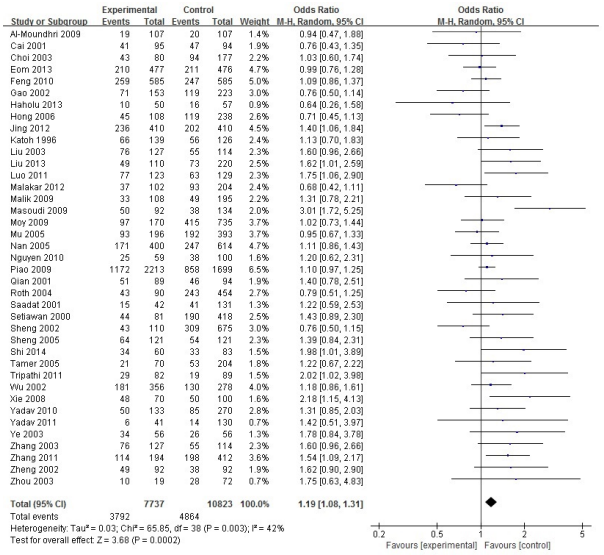

Figure 2. Forest Plots for the Association Between Null Genotype of GSTT1 and Gastric Cancer Risk. Boxes represent the ORs of individual studies, and diamonds represent the overall OR. Horizontal lines represent the 95% CI

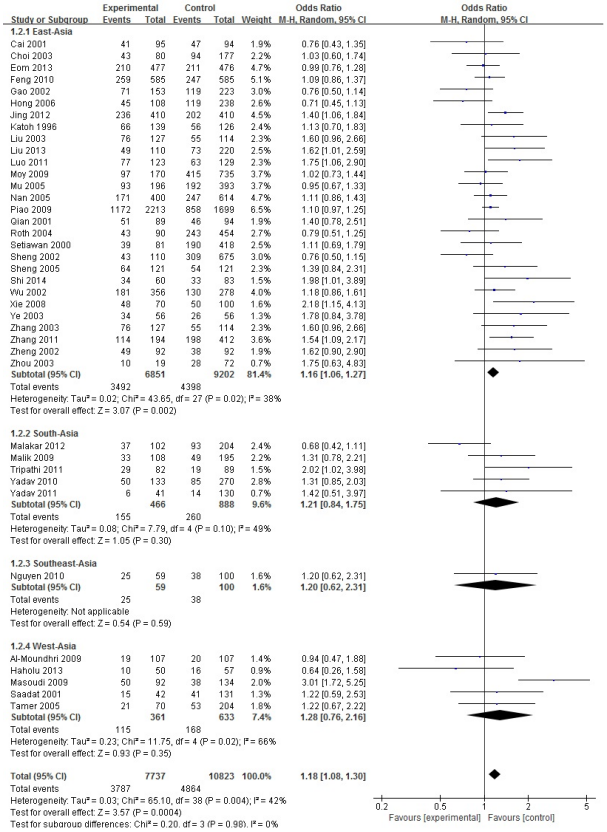

Figure 3. Forest Plots for the Subgroup Analysis by Subregion in the Meta-analysis

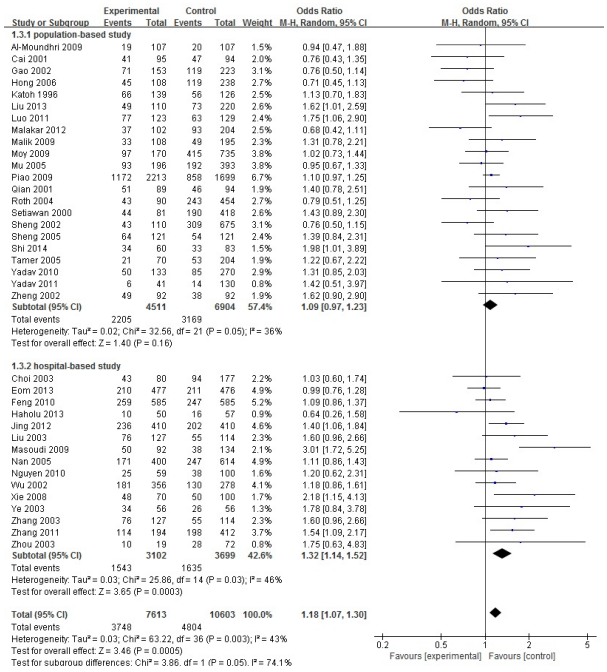

Figure 4. Forest Plots for the Subgroup Analysis by Study Design in the Meta-analysis.

infection status (Infection, OR=1.29, 95% CI=0.68-2.44, p=0.43; Non-infection, OR=1.17, 95% CI=0.50-2.75, p=0.72) and histology type (Diffuse, OR=0.92, 95% CI=0.66-1.29, p=0.64; Intestinal, OR=1.30, 95% CI=0.96-1.77, p=0.09) . The detailed data were listed in Table 3.

Publication bias

Inverted funnel plot and Egger's test were used to evaluate the potential publication bias in this meta-analysis. As shown in Figure 5, the shape of the funnel plots seemed approximately symmetrical for total studies analysis. Additionally, in the subgroup analyses by subregion the funnel plots also did not show any evidence of publication bias. In Egger's test the result also revealed the absence of publication bias in the *GSTT1* (p>0.05 for Null vs. Non-null model). Briefly, there was no risk of publication bias in this meta-analysis.

Sensitivity analysis

Sensitivity analysis was analyzed by sequentially excluding individual case-control study. The statistically similar results were obtained, which suggest the results of this meta-analysis are stable (Data were not shown

Discussion

Gastric cancer is a multistage process caused by

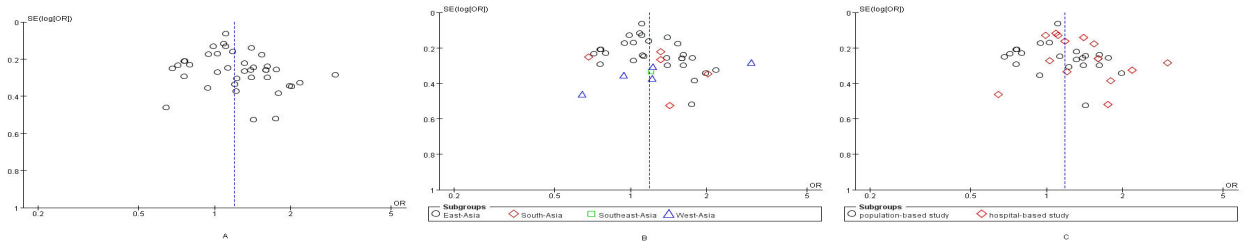

Figure 5. Inverted Funnel Plot for Publication Bias in Selection of Studies on Null Genotype of GSTT1. A overall, B subgroup analysis by subregion, C subgroup analysis by study design

multifarious factors that environmental and genetic factors may all contribute to the etiology of this carcinoma (Al-Moundhri et al., 2009). The relationship between polymorphisms in genes which encode proteins involving in carcinogens metabolism and individual susceptibility to carcinogenic impacts of the specific chemical compound is a new and concern field of research. *GSTT1* is one class of glutathione S-transferases (GSTs)-one type of biotransformation enzymes, which is appear in most epithelial tissues of the human gastrointestinal tract. The presumptive function of *GSTT1* is to protect tissues resist toxic or carcinogenic compounds that may enter to human body through the digestive tract or respiratory system (Qian et al., 2001). At present, the association between the *GSTT1* genetic polymorphisms and susceptibility to gastric cancer has been conflicting. Accordingly, we performed a meta-analysis, a quantitative research method increasing sample size and statistical significance, to estimate whether null genotype in *GSTT1* gene associated with gastric cancer risk. Finally, we conducted 39 published studies including 7737 cases and 10823 controls, which met the inclusion criteria for the meta-analyses. In overall combination studies, the results indicated that null polymorphism of *GSTT1* is associated with a significant increase in the risk of gastric cancer. In the subgroup analysis by subregion, the *GSTT1* null genotype was associated with an increased risk of gastric cancer in East Asian population but not in South Asian, Southeast Asian and West Asian population, which consistent with the statistical result performed by Jemal in 2011 (Jemal et al., 2011). Possible explanation to these different results may be that different genetic backgrounds and environmental exposures might play a key role in the development of gastric cancer. Furthermore, significantly increased gastric cancer risk was found in hospital-based design but not in population-based design. Such result may due to the biases in hospital-based design, the genotype distributions in hospital-based design could not represent the general population very well. In the subgroup analysis of smoking status and alcohol status, it is worthy to mention the inconsonant results which differ with a previous meta-analysis performed by Wang et al (Wang et al., 2014). In Wang's study, *GSTT1* null genotype has a significantly increased gastric cancer risk among smokers and alcohol drinkers. Inversely, results of our study indicated the lack of association between *GSTT1* null genotype and gastric cancer among smoker and alcohol drinker. The controversial results might due to the huge difference in simple size mainly. The other explanation to these different results may be that the difference or uniform definition of smoking and alcohol drinking in each study suggesting uncertain influence among smoker and alcohol drinker. Previous study suggested that *H. pylori* infection plays a central role in the gastric cancer carcinogenesis (Trajkov et al., 2007). Although *H. pylori* infection is independent risk factor for gastric cancer, there was no evidence to suggest an interaction between *GSTT1* null polymorphism and this risk factor in the present study. Possible explanation to such result may be the limitation of studies because studies with small sample had insufficient statistical power to detect a slight effect. In this meta-analysis, only three studies involving 259 cases and 720 controls examined the interaction of the *GSTT1* null genotype and the *H. pylori* infection status in gastric cancer patients. Considering the limited studies, our result should be interpreted with caution. Therefore, more relevant data are needed to confirm this finding.

Some issues which may affect the results should be addressed when performing meta-analysis, such as heterogeneity, sensitivity analysis and publication bias. In our study, heterogeneity existed in overall comparisons. After carrying out sensitivity analysis by sequentially excluding individual studies, we found that the results of our meta-analysis are stable. Hence a random effect model was performed to pooling data. Publication bias is another important issue that may influence the results of meta-analysis, which also be discussed in the present study. In this meta-analysis, both examination results of Inverted funnel plot and Egger's test were indicated that there was no risk of publication bias in this meta-analysis (Inverted funnel plot seemed approximately symmetrical and p=0.675 for Egger's test).

To our knowledge, there was a recently published study by Zhang in 2013 (Zhang et al., 2013). They also focus on the correlation of *GSTT1* genetic polymorphisms with gastric cancer risk in the Asian population. But there are differences between these two studies. First, the present meta-analysis updates the recent data for this polymorphism and gastric cancer risk and includes more studies than Zhang's study, which possibly providing more reliable conclusions; Second, more subgroups of meta-analysis were addressed in our study, such as subregion group, smoking status, alcohol status, *H. pylori* infection status and histology type. Although these differences, our study also indicated the null genotype of *GSTT1* might contribute to the risk of gastric cancer, which is consistent with Zhang's study results.

In summary, the present meta-analysis suggested that null variant in the *GSTT1* gene may contribute to gastric cancer risk. However, we have to mention several limitations of this study. First, a literature search just carried out in the selected databases; second, only published studies in Chinese and English were included for data analysis. For these reasons, some potential studies included by other databases or published in other languages or unpublished could be missed. In addition, due to lack of available data, the possible interaction of gene-environment could not be evaluated accurately. Accordingly, larger well-designed studies are warranted to verify these results. Moreover, gastric cancer carcinogenesis undergoes a complex progression from the development of chronic inflammation to acute neoplasias (Macarthur et al., 2004). Thus, further studies investigating *GSTT1* polymorphisms for gastritis should be performed.

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