Int J Clin Exp Med 2019;12(3):2912-2920
www.ijcem.com /ISSN:1940-5901/IJCEM0087830

Original Article

Meta-analysis of the association between the rs9282861 polymorphism in SULT1A1 and digestive tract cancer risk

Jia Zhu[1*], Yaxiong Liu[1*], Peng Du[1], Chong He[1], Gang Hu[1], Sen Li[1], Meiyu Ye[1], Jinsheng Zeng[1], Qiuhong Tian[2]

[1]Department of General Surgery, The First Affiliated Hospital, Nanchang University, Nanchang 330000, Jiangxi, China; [2]Department of Oncology, The First Affiliated Hospital, Nanchang University, Nanchang 330000, Jiangxi, China. [*]Co-first authors.

Received November 3, 2018; Accepted December 10, 2018; Epub March 15, 2019; Published March 30, 2019

Abstract: Recent studies have shown that *SULT1A1* rs9282861 polymorphism was associated with many types of cancer risk. While there was no meta-analysis on *SULT1A1* rs9282861 polymorphism would lead to increase the risk of digestive tract cancer. In order to better understanding the association between this snp and digestive tract cancer risk, we summarized available data and performed this meta-analysis. The pooled odds ratios (ORs) with their 95% confidence interval (95% CIs) were calculated to assess the associations. Beggs funnel plots was used to evaluate publication bias. A total of 22 studies including 7397 cancer patients and 10378 controls were analyzed. Overall, this meta-analysis revealed *SULT1A1* rs9282861 polymorphism was associated with an increased risk of digestive tract cancer under dominant model (GA+AA vs GG OR=1.08, 95% CI=1.02-1.15, P=0.013), allelic model: (A vs G OR=1.20, 95% CI=1,07-1.33, P=0.001). In subgroup analyses, significant associations were observed between SULT1A1 rs9282861 polymorphism and upper aero digestive tract (UADT) cancer under dominant model (GA+AA vs GG OR=1.32, 95% CI=1.14-1.52, P=0.010), recessive model (AA vs GA+GG OR=1.63, 95% CI=1.19-2.23, P=0.002), homozygous model (AA vs GG OR=1.60, 95% CI=1.20-2.15, P=0.001), allelic model: (A vs G OR=1.53, 95% CI=1.07-2.00, P=0.002). While no associations were detected between *SULT1A1* rs9282861 and crectal cancer. To sum up, this meta-analysis indicated that *SULT1A1* rs9282861 (Arg213His) polymorphism was associated with digestive cancer, indicating that *SULT1A1* rs9282861 polymorphism may serves as a digestive tract cancer tumor susceptibility marker. In subgroup analysis, it contributed to UADT (upper aero digestive tract) cancer, whereas no association were found between *SULT1A1* rs9282861 polymorphism and colorectal cancer.

Keywords: rs9282861 polymorphism in SULT1A1 meta-analysis digestive tract cancer risk colorectal cancer (CRC) UADT(upper aero digestive tract) cancer

Introduction

Digestive tract cancers (including esophageal, gastric and colorectal cancers), well known as the most common malignant tumours globally, include upper aero digestive tract and colorectal cancers [1-4]. Esophageal, gastric and colorectal cancers are the leading causes of cancer-related death in Eastern Asian countries [2, 3].

Sulfotransferase (SULT) enzymes catalyze the sulfate conjugation of a broad range of substrates and play an important role in metabolism of endogenous and exogenous compounds including thyroid and steroid hormones, neurotransmitters, drugs and pro-carcinogens [5, 6]. There are many isoforms of the SULTs supergene family, each with different amino acid sequence identity and substrate specificity [7]. The *SULT1A1* gene is located on chromosome 16p12.1-p11.2 [8]. *SULT1A1* is expressed in the liver, as well as in many extrahepatic tissues (e.g colonic mucosa), and is a component in the detoxification pathway of numerous xenobiotics [9]. Recent study has demonstrated a G to A transition at nucleotide 638 in *SULT1A1* gene causes an Arg to His substitution associated with a low enzymatic activity, which leads to individual·s susceptibility to can-

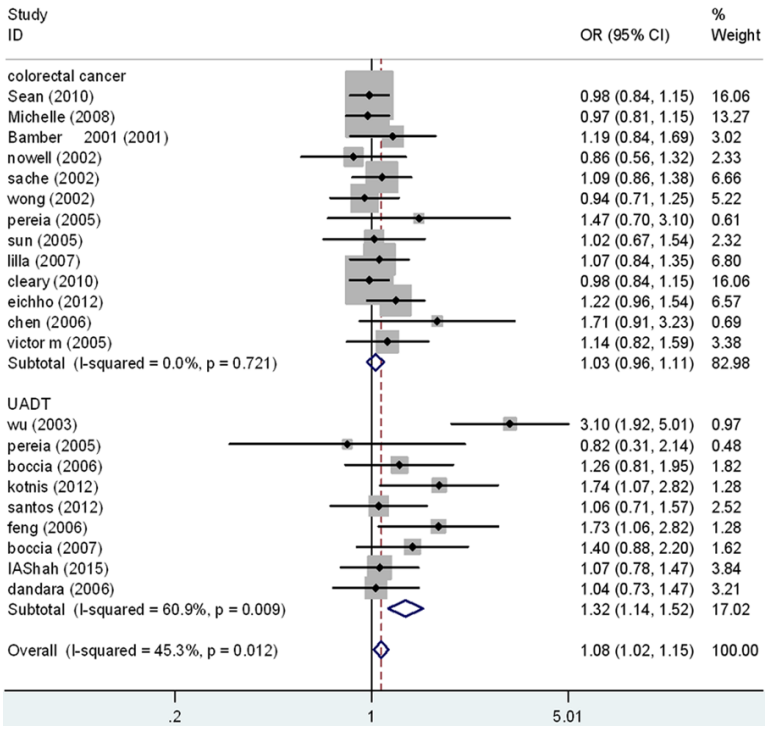

Figure 1. Forest plot on the association between SULT1A1 rs9282861 polymorphism and digestive tract cancer risk in dominant model.

cer [10, 11]. Many studies have demonstrated that this polymorphism played a significant role in the susceptibility to several cancers. A meta-analysis has revealed the association between *SULT1A1* rs9282861 polymorphism and the risk of UADT cancer [12]. Another study investigated the association between *SULT1A1* rs9282861 polymorphism and colorectal cancer risk showed that *SULT1A1* rs9282861 polymorphism lacks of association with colorectal cancer [13]. Whereas there was no meta-analysis about the association between *SULT1A1* rs9282861 and digestive tract cancer. Thus we wounder that whether *SULT1A1* rs9282861 polymorphism would increase or decrease digestive tract cancer risk. So as to better understand the association, we performed this Meta-analysis to explore the overall relationship between this polymorphism and digestive tract cancer risk.

Material and methods

Identification of eligible studies

Electronic searches of Pubmed, PMC, and CNKI were performed for all publications on the associations of *SULT1A1* rs9282861 and digestive cancer from 2000 to 2017. Using *"SULT1A1"*, "rs9282861", "R213H", "Arg213His", "digestive tract", "UADT", "esophageal", "gastric", "liver", "colorectal", "snp", "neoplasms" OR "cancer" as key words. Searching was conducted by two independent researchers to make sure that no published papers were missed. No language restrictions were applied. The eligible studies must meet the following requirements: (1) case-control studies focused on the associations of *SULT1A1* rs9282861 polymorphisms with liver, gastric, colorectal, esophagus risk (2) detailed data (including genotype frequencies of *SULT1A1* rs9282861 polymorphism) for calculating odds ratio (OR) with 95% confidence interval (95% CI) (3) all of the cases and controls SNPs conformc to the Hardy-Weinberg equilibrium (HWE). We excluded studies overlapping with other studies or overlapping with data from the same authors.

Data extraction

Two authors (Zhu and Liu) independently extracted the data. For each case, if there was disagreement, the two authors debated until the agreement was reached on all items. The following information was collected: the first author's name, year of publication, cancer type, ethnicity, numbers of cases and controls, source of the study population. If a study included many tumor types, genotype data were extracted separately according to tumor type.

Statistical analysis

We calculated the odds ratio (OR) with 95% confidence interval (CI) to access the association between the SULT1A1 rs9282861 polymorphism and digestive tract. The heterogeneity was assessed by the Chisquare based Q statistics and I^2 test. Heterogeneity was considered significantly at either a *P* value of <0.10 or I^2>50%. When heterogeneity was detected among the studies, the random-effects (the

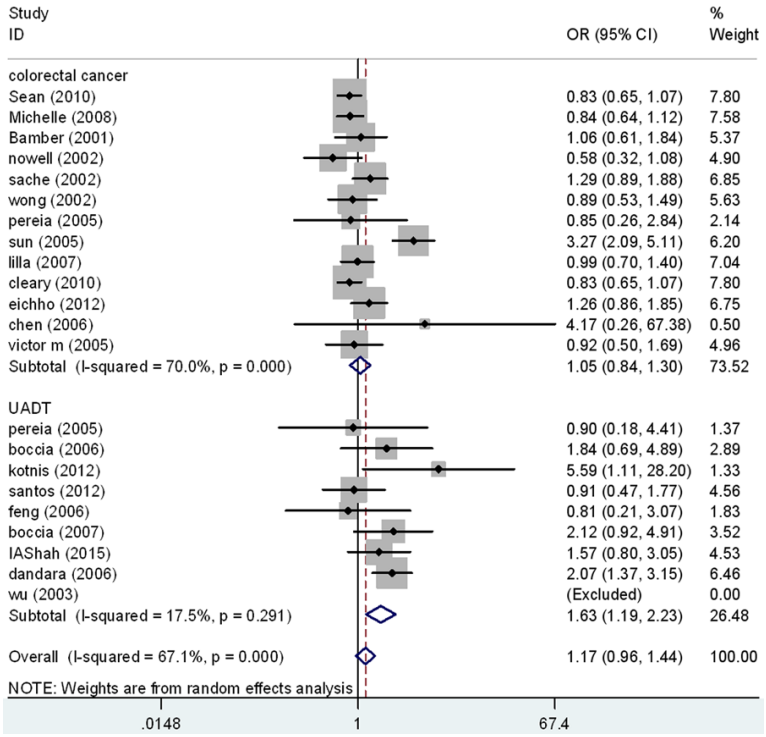

Figure 2. Forest plot on the association between SULT1A1 rs9282861 polymorphism and digestive tract cancer risk in recessive model.

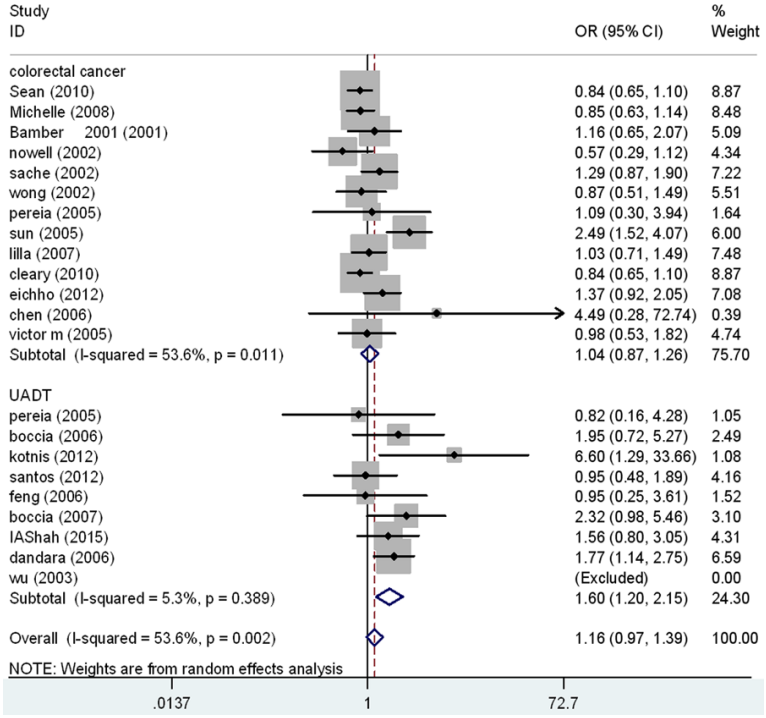

Figure 3. Forest plot on the association between SULT1A1 rs9282861 polymorphism and digestive tract cancer risk in homozygous model.

DerSimonian and Laird method) model instead of the fixed-effects model (the Mantel-Haenszel method) was applied to estimate the pooled OR.

Publication bias and sensitivity analysis

We used Beggs funnel plots to evaluatey the publication bias of this studies. What we can see from the picture (**Figure 6**) shows that the studies including in this meta-analysis indicate no publication bias. We removed each study repeatedly to measure the sensitivity analysis. The corresponding pooled ORs were not changed significantly, indicating that our results were statistically valid.

Results

Characteristics of studies

In this meta-analysis, 22 studies from 20 articles **Figure 7** [13-32] were identified to evaluate the relationship between *SULT1A1* rs9282861 polymorphisms and risk of digestive tract cancer, and a total number of 7397 cases and 10378 controls were included [14-33]. There are 13 studies on colorectal cancer, 5 studies reported information on UADT, 2 studies on gastric cancer and esophagus cancer respectively. The relevant characteristics of studies were listed in **Table 1**.

Overall meta-analysis results

Table 2 lists the main consequences of the pooled analyses. Overall, As you can see from **Table 2**, the *SULT1A1* rs9282861 polymorphism was associated with an increased risk of digestive tract cancer under dominant model **Figure 1** (GA+AA vs GG OR=1.08, 95% CI=1.02-1.15, P=0.013), recessive model **Figure 2** (AA vs GA+GG OR=1.17 95% CI=0.96-

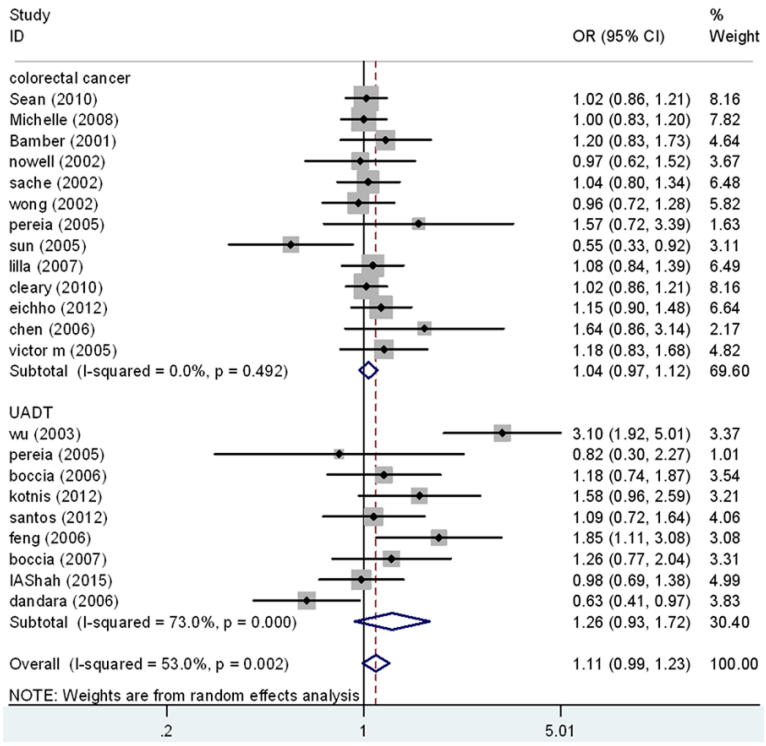

Figure 4. Forest plot on the association between SULT1A1 rs9282861 polymorphism and digestive tract cancer risk in heterozygous model.

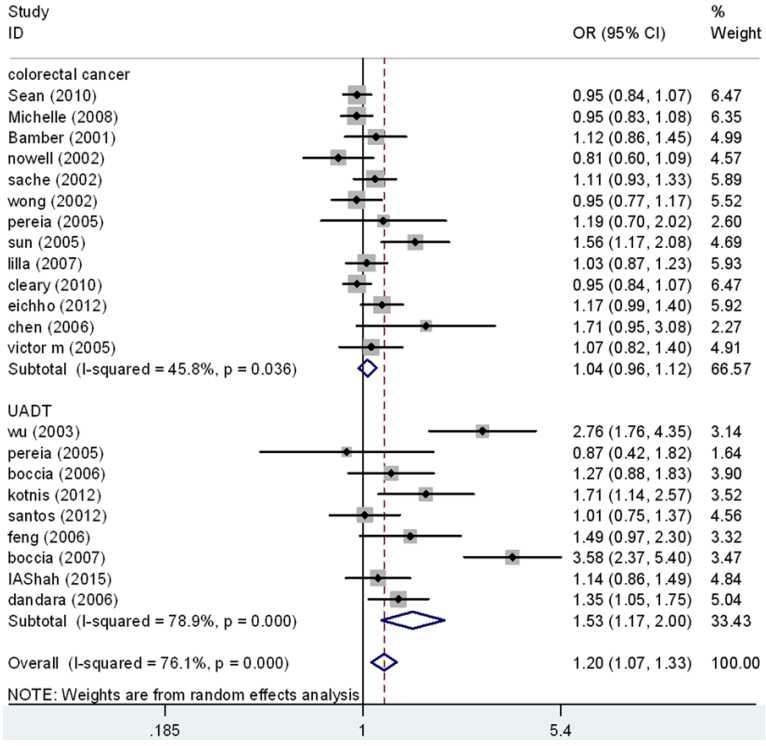

Figure 5. Forest plot on the association between SULT1A1 rs9282861 polymorphism and digestive tract cancer risk in allelic model.

1.44 P=0.122), homozygous model **Figure 3** (AA vs GG OR=1.16 95% CI=0.97-1.39 P=0.099), heterozygous model **Figure 4** (GA vs GG OR= 1.11 95% CI=0.99-1.23 P= 0.067) and allelic model **Figure 5** (A vs G OR=1.20, 95% CI=1,07-1.33, P=0.001).

Subgroup meta-analysis results

Table 3 showed that *SULT1A1* rs9282861 is not linked with colorectal cancer under dominant model (GA+AA vs GG OR=1.03, 95% CI=0.96-1.11, P=0.013), recessive model (AA vs GA+GG OR=1.05, 95% CI=0.84-1.30 P=0.684), homozygous model (AA vs GG OR=1.04, 95% CI=0.97-1.12, P=0.655), heterozygous model (GA vs GG OR=1.04 95% CI=0.97-1.12 P=0.297), allelic model: (A vs G OR=1.04, 95% CI=0.96-1.12, P=0.325). **Table 4** shows *SULT1A1* rs9282861 was statistically significant with increased risk of UADT cancer under dominant model (GA+AA vs GG OR=1.32, 95% CI=1.14-1.52, P=0.010), recessive model (AA vs GA+GG OR=1.63, 95% CI=1.19-2.23, P=0.002), homozygous model (AA vs GG OR=1.60, 95% CI= 1.20-2.15, P=0.001), heterozygous model (GA vs GG OR=1.26 95% CI=0.93-1.72 P=0.137), allelic model: (A vs G OR=1.53, 95% CI=1.07-2.00, P=0.002).

Discussion

To the best of our knowledge, this is the first meta-analysis about the association between *SULT1A1* rs9282861 polymorphism and digestive tract cancer. This meta-analysis including 7506 cases and 11044 controls from 22 stud-

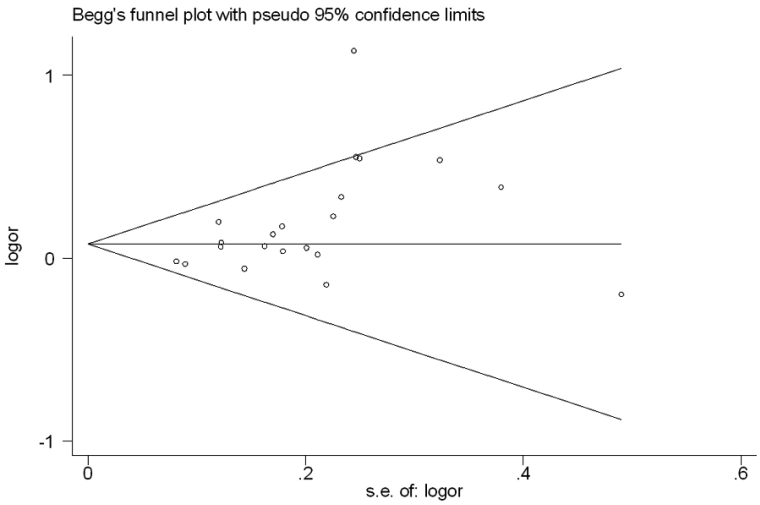

Figure 6. Beggs funnel plot with pseudo 95% confidence limits.

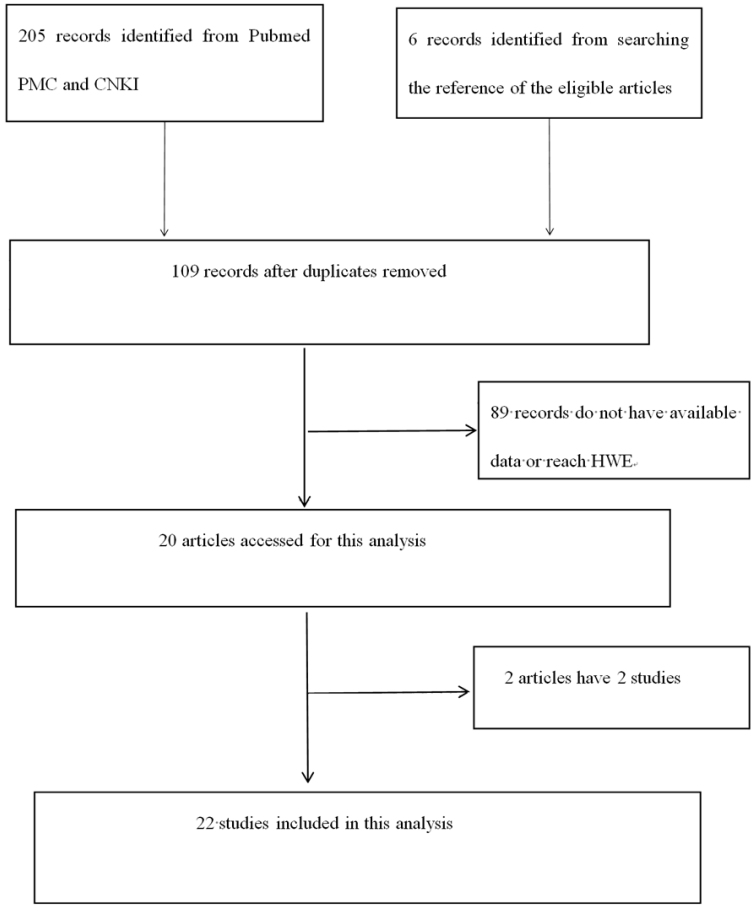

Figure 7. Processes of study selection.

ies, explored the association between the *SULT1A1* rs9282861 polymorphism and digestive tract cancer risk. Our meta-analysis revealed that *SULT1A1* rs9282861 polymorphism contribute to digestive tract cancer under dominant model, allelic model.

SULT1A1 enzyme encoded by SULT1A1 gene plays an important role in xenobiotic metabolism. Previous studies have demonstrated that *SULT1A1* is an important member of the sulfotransferase family involving in the pathogenic process of various cancers [7, 33, 34]. First, *SULT1A1* is known to catalyze the sulfation of not only dietary carcinogens such as the heterocyclic aromatic amines (HAAs), but also that of several dietary chemopreventives such as catechins [35]. In addition, Previous study indicated that A functiona lpolymorphism in exon 7 of the SULT1A1 gene, with a G⟶A substitution, results in a change in the amino acid sequence from arginine to histidine, leading to a decrease in enzymatic activity [33, 36]. Carriers of the GG and GA allele of SULT1A1 are defined as having normal enzyme activity, the AA allele as having decreased activity which is associated with susceptibility to several cancers [36]. However the mechanism of *SULT1A1* rs9282861 polymorphism increasing digestive tract cancers is unclear so far. Therefore we performed this meta-analysis to explore the association between the *SULT1A1* rs9282861 polymorphism and digestive tract cancers risk.

There are many studies focuses on the association between *SULT1A1* rs9282861 polymorphism and digestive tract cancers. Boccia [20] and Feng [26] indicated that the strongly positive association between *SULT1A1* rs9282861 polymorphism and UADT.

Table 1. Characteristics of the included studies

First author's name	Year	Cancer type	Ethnicity	Sample Size (Case/Control)	Genotype Distribution (Case/Control)		
					GG	GA	AA
Sean	2010	Colorectal cancer	Caucasian	1164/1292	544/598	502/540	118/154
Michelle	2008	Colorectal cancer	Caucasian	834/1249	396/578	353/523	85/148
Bamber	2001	Colorectal cancer	Caucasian	226/293	96/137	104/124	26/32
Nowell	2002	Colorectal cancer	Mixed	130/301	48/101	67/145	15/55
Sache	2002	Colorectal cancer	Caucasian	490/593	217/275	209/255	64/63
Wong	2002	Colorectal cancer	Caucasian	383/402	175/178	179/190	29/34
Wu	2003	UADT	East Asians	187/308	135/274	52/34	0/0
Pereia	2005	Colorectal cancer	Mixed	42/100	15/45	23/44	4/11
Pereia	2005	UADT	Mixed	20/100	10/45	8/44	2/11
Sun	2005	Colorectal cancer	Caucasian	109/666	43/266	27/303	39/97
Boccia	2006	UADT	Caucasian	123/247	71/156	44/82	8/9
Lilla	2007	Colorectal cancer	Caucasian	504/603	212/263	225/259	67/81
Cleary	2010	Colorectal cancer	Caucasian	1164/1292	118/154	502/540	118/154
Eichholzer	2012	Colorectal cancer	Caucasian	424/819	183/389	193/354	48/76
Kotnis	2012	UADT	India	109/194	60/132	43/60	6/2
Santos	2012	UADT	Mixed	202/196	94/94	89/82	19/20
Shen	2006	Colorectal cancer	East Asians	83/343	67/301	15/41	1/1
Feng	2006	UADT	East Asians	163/166	109/129	50/32	4/5
Boccia	2007	UADT	Caucasian	107/254	57/156	39/85	11/13
IAShah	2015	UADT	South Asians	404/404	300/305	81/84	23/15
Dandara	2006	UADT	South Africans	236/266	115/132	47/86	74/48
Victorm	2005	Colorectal cancer	Caucasian	293/272	163/160	107/89	23/23

Whereas Santos's [25] study revealed that *SULT1A1* rs9282861 polymorphism was not related to UADT. Pereira [18] found that *SULT1A1* rs9282861 polymorphism contributed to gastric cancer. Boccia draw the same conclusion as Pereira. Lilla [21] suggested that *SULT1A1* rs9282861 polymorphism was not linked with colorectal cancer. Cleary [22] found that there was also no statistically significant association between *SULT1A1* rs9282861 polymorphism and Colorectal cancer risk. Bamber [13] found that *SULT1A1* rs9282861 polymorphism could reduce the risk of colorectal cancer. Taken all into consideration, the association between *SULT1A1* rs9282861 polymorphism and digestive tract cancers is unknown. So we conducted this meta-analysis to explore the association between *SULT1A1* rs9282861 polymorphism and digestive tract cancers. According to this meta-analysis *SULT1A1* rs9282861 polymorphism increased the risk of digestive tract cancers especially UADT cancers. It may due to the fact that the upper aero digestive tract is exposed to numerous potential carcinogens such as phenolic xenobiotics, polycyclic aromatic hydrocarbons and heterocyclic aromatic amines contained in cigarette smoking, environmental pollutants and some food, this result manifests that the mutation within SULT1A1 causes the low SULT1A1 activity and is associated with high susceptibility to UADT cancer [12].

While no statistically significant association was observed between *SULT1A1* rs9282861 polymorphism and colorectal cancer risk. Though Sun [19] found that *SULT1A1* rs9282861 polymorphism was associated with colorectal cancer. Cheng [27] also found that *SULT1A1* rs9282861 polymorphism was related to colorectal cancer combing with high intake of red meat. Conversely, Wong [16] and Eichholzer [23] hold that *SULT1A1* rs9282861 polymorphism was not related to colorectal cancer. Recently, Xiao [12] conducted a meta-analysis that draw the conclusion and *SULT1A1* rs9282861 polymorphism was not related to colorectal cancer. As we know SULT1A1 is the

Table 2. Meta-analysis results of the association between SULT1A1 rs9282861 polymorphism and digestive tract cancer

Model	OR (95% CI)	I-squre (%)	P
Dominant model (GA+AA vs GG)	1.08 (1.02-1.15)	45.3	0.013
Recessive model (AA vs GA+GG)	1.17 (0.96-1.44)	67.1	0.122
Homozygous model (AA vs GG)	1.16 (0.97-1.39)	53.87	0.099
Heterozygous model (GA vs GG)	1.11 (0.99-1.23)	53.0	0.067
Allelic model (A vs G)	1.20 (1.07-1.33)	76.1	0.001

Table 3. Meta-analysis results of the association between SULT1A1 rs9282861 polymorphism and colorectal cancer

Model	OR (95% CI)	I-squre (%)	P
Dominant model (GA+AA vs GG)	1.03 (0.96-1.11)	0.0	0.354
Recessive model (AA vs GA+GG)	1.05 (0.84-1.30)	70.0	0.684
Homozygous model (AA vs GG)	1.04 (0.87-1.26)	53.87	0.65500
Heterozygous model (GA vs GG)	1.04 (0.97-1.12)	0.0	0.297
Allelic model (A vs G)	1.04 (0.96-1.12)	45.8	0.325

Table 4. Meta-analysis results of the association between SULT1A1 rs9282861 polymorphism and upper aero digestive tract cancer

Model	OR (95% CI)	I-squre (%)	P
Dominant model (GA+AA vs GG)	1.32 (1.14-1.52)	60.9	0.010
Recessive model (AA vs GA+GG)	1.63 (1.19-2.23)	17.5	0.002
Homozygous model (AA vs GG)	1.60 (1.20-2.15)	53.87	0.001
Heterozygous model (GA vs GG)	1.26 (0.93-1.72)	73	0.137
Allelic model (A vs G)	1.53 (1.07-2.00)	78.9	0.002

isoform primarily associated with the conversion of dietary N-OH arylamines to DNA binding adducts, Studies have indicated that the increased amounts of N-OH arylamines can increase the chance of colorectal cancer development [37]. However, our meta-analysis's results were consistent with Xiao's. The result is difficult to explain. Because there are many factors may influence the function of the polymorphism. One possible reason might be that the polymorphism plays different role in different organs or ethnic populations. It may also be that different parts of digestive tract flora influence function of the polymorphism. So further detailed investigation with larger number of worldwide participants is needed to better understand the role of this polymorphism in colorectal cancer risk and ethnicities.

These findings may help us better understand the *SULT1A1* rs9282861 polymorphism in the etiology of digestive system cancer. The *SULT1A1* rs9282861 polymorphism can be used as clinical reference, when we clinically diagnosed digestive system cancer. While we should take environment, age, gender, ethnicity, cancer types into consideration. As is known the effect of genetic constellation, the enzymatic activity can be influenced by environmental factors such as smoking and diet [38], but also by gene-gene interactions [39].

Despite the strength of our study that yielded enough power to implement a comprehensive analysis, there was a lot of room for improvement. First of all, the sample size of this meta-analysis was relatively small. Furthermore, the studies included in this meta-analysis lack of more detailed data (such as lifestyle, dietary habits), which may lead to precise result. Besides, we did not evaluate the interactions of gene-gene and gene-environment in all studies. Additionly due to the insufficient sample size used in this meta-analysis, we did not analyze the association between ethnicities and this polymorphism. Moreover, those researchs were conducted many years ago, more updated researchs are required to clarified the association between *SULT1A1* rs9282861 polymorphism and digestive tract cancers.

Conclusion

In conclusion, according to this meta-analysis, the association between the rs9282861 polymorphism in *SULT1A1* and digestive tract cancer risk was remarkable. Though *SULT1A1* rs9282861 polymorphism will increase the risk of digestive tract cancer, the risk relyes on the type of cancer. In the future, more studies with larger sample sizes that further assess the role of *SULT1A1* rs9282861 polymorphism in risk of digestive tract cancer may help us understand more about the association.

Acknowledgements

This work was supported by Science Technology Department of Jiangxi provincial (20112BBG-70051) and Education Department of Jiangxi (GJJ14041).

Disclosure of conflict of interest

None.

Address correspondence to: Jinsheng Zeng, Department of General Surgery, The First Affiliated Hospital, Nanchang University, Nanchang 330000, Jiangxi, China. E-mail: zengjinsheng0606@163.com; Qiuhong Tian, Department of Oncology, The First Affiliated Hospital, Nanchang University, Nanchang 330000, Jiangxi, China. E-mail: enanchang@163.com

References

[1] Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J and Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015; 65: 87-108.

[2] Peleteiro B, Castro C, Morais S and Ferro A. Worldwide burden of gastric cancer attributable to tobacco smoking in 2012 and predictions for 2020. Dig Dis Sci 2015; 60: 2470-2476.

[3] Lakhoo K. Neonatal surgical conditions. Early Hum Dev 2014; 90: 933.

[4] Zhang JM, Cui XJ, Xia YQ, and Guo S. Correlation between TGF-beta1-509 C>T polymorphism and risk of digestive tract cancer in a meta-analysis for 21,196 participants. Gene 2012; 505: 66-74.

[5] Coughtrie MW. Sulfation through the looking glass-recent advances in sulfotransferase research for the curious. Pharmacogenomics J 2002; 2: 297-308.

[6] Richard K, Hume R, Kaptein E, Stanley EL, Visser TJ, Coughtrie MW. Sulfation of thyroid hormone and dopamine during human development: ontogeny of phenol sulfotransferases and arylsulfatase in liver, lung, and brain. J Clin Endocrinol Metab 2001; 86: 2734-2742.

[7] Glatt H. Sulfotransferases in the bioactivation of xenobiotics. Chem Biol Interact 2000; 129: 141-170.

[8] Dooley TP and Huang Z. Genomic organization and DNA sequences of two human phenol sulfotransferase genes (STP1 and STP2) on the short arm of chromosome 16. Biochem Biophys Res Commun 1996; 228: 134-140.

[9] Harris RM, Picton R Singh S and Waring RH. Activity of phenol sulfotransferases in the human gastrointestinal tract. Life Sci 2000; 67: 2051-5710

[10] Nagar S, Walther S and Blanchard RL. Sulfotransferase (SULT) 1A1 polymorphic variants *1, *2, and *3 are associated with altered enzymatic activity, cellular phenotype, and protein degradation. Mol Pharmacol 2006; 69: 2084-2092.

[11] Ozawa S, Tang YM, Yamazoe Y, Kato R, Lang NP and Kadlibar FF. Genetic polymorphisms in human liver phenol sulfotransferases involved in the bioactivation of N-hydroxy derivatives of carcinogenic arylamines and heterocyclic amines. Chem Biol Interact 1998; 109: 237-48.

[12] Xiao JJ, Zheng YB, Zhou YH, Zhang P, Wang JG, Shen FY, Fan LX, Kolluri VK, Wang WP, Yan XL and Wang MH. Sulfotransferase SULT1A1 Arg213His polymorphism with cancer risk: a meta-analysis of 53 case-control studies. PLOS One 2014; 9: e106774.

[13] Bamber DE, Fryer AA, Strange RC, Elder JB, Deakin M, Rajagopal R, Fawole A, Gilissen RA, Campbell FC and Coughtrie MW. Phenol sulphotransferase SULT1A1*1 genotype is associated with reduced risk of colorectal cancer. Pharmacogenetics 2001; 11: 679-685.

[14] Nowell S, Coles B, Sinha R, MacLeod S, Luke Ratnasinghe D, Stotts C, Kadlubar FF, Ambrosone CB and Lang NP. Analysis of total meat intake and exposure to individual heterocyclic amines in a case-control study of colorectal cancer: contribution of metabolic variation to risk. Mutat Res 2002; 506-507: 175-185.

[15] Sachse C, Smith G, Wilkie MJ, Barrett JH, Waxman R, Sullivan F, Forman D, Bishop DT and Wolf CR. A pharmacogenetic study to investigate the role of dietary carcinogens in the etiology of colorectal cancer. Carcinogenesis 2002; 23: 1839-1849.

[16] Wong CF, Liyou N, Leggett B, Young J, Johnson A and McManus ME. Association of the SULT1A1 R213H polymorphism with colorectal cancer. Clin Exp Pharmacol Physiol 2002; 29: 754-758.

[17] Wu MT, Wang YT, Ho CK, Wu DC, Lee YC, Hsu HK, Kao EL, Lee JM. SULT1A1 polymorphism and esophageal cancer in males. Int J Cancer 2003; 103: 101-104.

[18] Pereira WO, Paiva AS, Queiroz JW, Toma L, Dietrich CP, Nader HB, Jerônimo SM. Genetic polymorphism in the sulfotransferase SULT1A1 gene in cancer. Cancer Genet Cytogenet 2005; 160: 55-60.

[19] Sun XF, Ahmadi A, Arbman G, Wallin A, Asklid D and Zhang H. Polymorphisms in sulfotransferase 1A1 and glutathione S-transferase P1 genes in relation to colorectal cancer risk and patients' survival. World J Gastroenterol 2005; 11: 6875-6879.

[20] Boccia S, Sayed-Tabatabaei FA, Persiani R, Gianfagna F, Rausei S, Arzani D, Greca AL, D'Ugo D, Torre GL, Duijn CM and Ricciardi G.

Polymorphisms in metabolic genes, their combination and interaction with tobacco smoke and alcohol consumption and risk of gastric cancer: a case-control study in an Italian population. BMC Cancer 2007; 7: 206.

[21] Lilla C, Risch A, Verla-Tebit E, Hoffmeister M, Brenner H and Chang-Claude J. SULT1A1 genotype and susceptibility to colorectal cancer. Int J Cancer 2006; 120: 201-206.

[22] Cleary SP, Cotterchio M, Shi E, Gallinger S, Harper P. Cigarette smoking, genetic variants in carcinogen-metabolizing enzymes, and colorectal cancer risk. Am J Epidemiol 2010; 172: 1000-1014.

[23] Eichholzer M, Rohrmann S, Barbir A, Hermann S, Teucher B Kaaks R and Linseisen J. Polymorphisms in heterocyclic aromatic amines metabolism-related genes are associated with colorectal adenoma risk. Int J Mol Epidemiol Genet 2012; 3: 96-106.

[24] Kotnis A, Namkung J, Kannan S, Jayakrupakar N, Park T, Sarin R and Mulherkar R. Multiple pathway-based genetic variations associated with tobacco related multiple primary neoplasms. PLoS One 2012; 7: 300-313.

[25] Santos SS, Koifman RJ, Ferreira RM, Diniz LF, Brennan P, Boffetta P and Koifman S. SULT1A1 genetic polymorphisms and the association betwee smoking and oral cancer in a case-control study in brazil cancer epidemiology and prevention. Fronti Oncol 2012; 2: 183.

[26] Feng XX, Zhu SJ, Wang LB, Duan ML, Zhang JB and Li PZ. Relationship between SULT1A1 gene polymorphisms and susceptibility to esophageal cancer. Chinesse Journal of Disease Control & Prevetion 2006; 10: 373-376.

[27] Chen K, Fan CH, Jin MJ, Song L, Xu H, He HQ and Tong F. [A case-control study on the association between the genetic polymorphism of sulfotransferase 1A1, diet and susceptibility of colorectal cancer]. Zhonghua Zhong Liu Za Zhi 2006; 28: 670-673.

[28] Cleary SP, Cotterchio M, Shi E, Gallinger S, Harper P. Cigarette smoking, genetic variants in carcinogen-metabolizing enzymes, and colorectal cancer risk. Am J Epidemiol 2010; 172: 1000-1014.

[29] Cotterchio M, Boucher BA, Manno M, Gallinger S, Okey AB, Harper PA. Harper red meat intake, doneness, polymorphisms in genes that encode carcinogen-metabolizing enzymes and colorectal cancer risk. Cancer Epidemiol Biomarkers Prev 2008; 17: 3098-3107.

[30] Dandara C, Li DP, Waither G and Parker MI. Gene-environment interaction: the role of SULT1A1 and CYP3A5 polymorphisms as risk modifiers for squamous cell carcinoma of the oesophagus. Carcinogenesis 2006; 27: 791-797.

[31] Shah IA, Bhat GA, Mehta P, Lone MM, Dar NA. Genotypes of CYP1A1, SULT1A1 and SULT1A2 and risk of squamous cell carcinoma of esophagus: outcome of a case-control study from kashmir, India. Dis Esophagus 2016; 29: 937-943.

[32] Moreno V, Glatt H, Guino E, Fisher E, Meinl W, Navarro M, Badosa JM and Boeing H. Polymorphisms in sulfotransferases SULT1A1 and SULT1A2 are not related to colorectal cancer. Int J Cancer 2005; 113: 683-686.

[33] Raftogianis RB, Wood TC, Otterness DM, Van Loon JA and Weinshilboum RM. Phenol sulfotransferase pharmacogenetics in humans: association of common SULT1A1 alleles with TS PST phenotype. Biochem Biophys Res Commun 1997; 239: 298-304.

[34] Glatt H. Sulfation and sulfotransferases 4: bioactivation of mutagens via sulfation. FASEB J 1997; 11: 314-321.

[35] Coughtrie M and Johnston L. Interactions between dietery chemicals and human sulfotransferases- molecular mechanisms and clinical significance. Drug Metab Dispos 2001; 29: 522-528.

[36] Engelke CE, Meinl W, Boeing H and Glatt H. Association between functional genetic polymorphisms of human sulfotransferases 1A1 and 1A2. Pharmacogenetics 2000; 10: 163-169.

[37] Chou HC, Lang NP and Kadlubar FF. Metabolic activation of N-hydroxy-arylamines and N-hydroxy heterocyclic amines by human sulfotransferase(s). Cancer Res 1995; 55: 525-529.

[38] Vvan der Logt EM, Bergevoet SM, Roelofs HM, van Hooijdonk Z, Te Morsche RH, Wobbes T, De Kok JB, Nagengast FM, Peters WH. Genetic polymorphisms in UDP-glucuronosyltransferases and glutathione S-transferases and colorectal cancer risk. Carcinogenesis 2004; 25: 2407-2415.

[39] Wang J, Jiang J, Zhao Y, Gajalakshmi V, Kuriki K, Suzuki S, Nagaya T, Nakamura S, Akasaka S, Ishikawa H and Tokudome S. Genetic polymorphisms of glutathione S-transferase genes and susceptibility to colorectal cancer: a case-control study in an Indian population. Cancer Epidemiol 2011; 35: 66-72.