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Review

Associations of the IL-17A rs2275913 and IL-17F rs763780 polymorphisms with the risk of digestive system neoplasms: A meta-analysis

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ABSTRACT

Objective: To clarify the associations between the IL-17A rs2275913 and IL-17F rs763780 polymorphisms and the risk of digestive system neoplasms.

Methods: An internet search was used to identify relevant articles from CNKI, Wanfang, VIP, PubMed, EMBASE and Elsevier up to December 2017. The meta-analysis was performed using Stata 11.0 software.

Results: Twenty-three studies were included. Among these, 21 studies with 6978 cases and 8000 controls were related to IL-17A rs2275913, while 18 studies that included 5073 cases and 6040 controls were related to IL-17F rs763780. The meta-analysis results demonstrated that the overall effects of the two polymorphisms were significantly different ($P < 0.05$) in the allele model, dominant model, recessive model and codominant model. Subgroup analysis showed that both polymorphisms were significantly associated with susceptibility to gastric cancer but not with hepatocellular carcinoma or colorectal cancer. In the ethnicity analysis, these two polymorphisms were associated with Asian populations but not with Caucasians. Similar results were observed in the hospital-based and population-based control subgroups.

Conclusions: The IL-17A rs2275913 and IL-17F rs763780 polymorphisms were associated with susceptibility to digestive system neoplasms.

1. Introduction

Digestive system neoplasms, due to their different locations within the organs and tissues associated with the gastrointestinal tract, have high morbidity and mortality rates, which pose a major threat to human health and severely affect normal life [1]. Common neoplasms in the digestive system include gastric cancer (GC), hepatocellular carcinoma (HCC), colorectal cancer (CRC), and esophageal cancer (EC), among others [2]. Genetic factors and environmental factors have an important influence on the occurrence of digestive system neoplasms; however, the specific mechanism remains unclear.

Interleukin-17 (IL-17) is a proinflammatory cytokine family that includes six members (IL-17A-F). IL-17 is secreted by activated $CD4^+$ T cells and neutrophils, and it not only plays an important part in autoimmune diseases, immune response against infections and graft rejection but also functions in the immune response to various malignancies [3]. In addition, IL-17 may also participate in antitumor and protumor processes [4]. Single nucleotide polymorphisms (SNPs) serve as important mutations that can affect transcription and translation. Numerous studies have reported the associations of IL-17A and IL-17F polymorphisms and susceptibility to digestive system neoplasms, especially GC; however, the results were not consistent. Therefore, we further expanded the sample size to research the relation between the two polymorphisms and the risk of digestive system neoplasms in terms of cancer type, ethnicity and controls.

2. Materials and methods

2.1. Study search strategy

Eligible studies published prior to December 2017 were obtained through three English databases (PubMed, EMBASE, Elsevier) and three Chinese databases (Chinese National Knowledge Infrastructure (CNKI), Wanfang, VIP), using the following key words: “interleukin-17A” or “IL-17A”, “interleukin-17F” or “IL-17F”, “polymorphism”, “gastric cancer”, “hepatocellular carcinoma”, and “colorectal cancer”.

2.2. Methods

The inclusion criteria were as follows: (1) studies of associations between IL-17A rs2275913 and IL-17F rs763780 polymorphisms and the susceptibility to digestive system neoplasms, such as GC, HCC and

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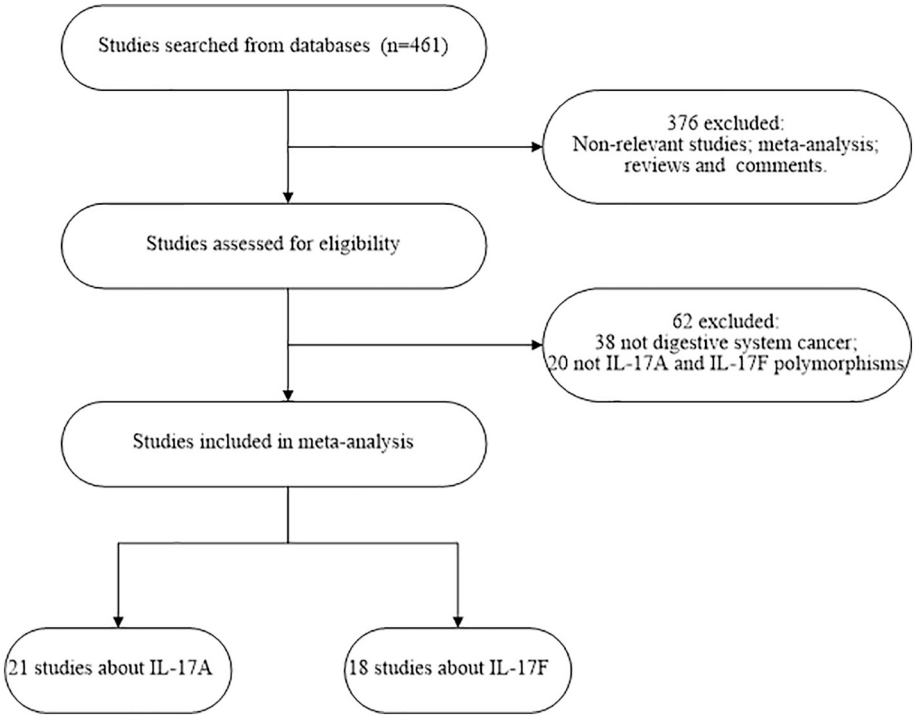

Fig. 1. Flow diagram of the literature selection process and results.

Table 1
Characteristics of the case-control studies included in the meta-analysis.

First author	Year	Country	Racial	Source of controls	Cancer Type	Case	Control	Genotyping method	No. of SNP
Zhao	2016	China	Asian	HB	GC	153	207	PCR-RFLP	1,2
Yang	2016	China	Asian	HB	GC	386	374	PCR-RFLP	1,2
Qi	2015	China	Asian	HB	GC	252	252	MassARRAY	1,2
Hou and Yang	2015	China	Asian	HB	GC	326	326	MassARRAY	1,2
Gao	2015	China	Asian	HB	GC	572	573	PCR-RFLP	1,2
Gao Wei	2015	China	Asian	PB	GC	386	374	PCR-RFLP	1,2
Zhang	2014	China	Asian	PB	GC	260	512	MassARRAY	1,2
Wang	2014	China	Asian	PB	GC	462	462	MassARRAY	1,2
Gonzalez-Hormazabal	2014	Mixed	Mixed	PB	GC	147	172	TaqMan	1,2
Zhu	2014	China	Asian	HB	GC	311	611	MassARRAY	1,2
Lan-qing Bi	2014	China	Asian	HB	GC	99	150	PCR-RFLP	1,2
Rafiei	2013	Iran	Caucasian	PB	GC	161	171	PCR-RFLP	1
Arisawa	2012	Japan	Asian	HB	GC	333	583	PCR-SSCP	1
Wu	2010	China	Asian	PB	GC	945	768	PCR-RFLP	1,2
Jian-jian Chen	2010	China	Asian	PB	GC	1042	1090	TaqMan	1
Luo	2010	China	Asian	HB	GC	24	230	PCR-RFLP	1,2
Shibata	2009	Japan	Asian	HB	GC	287	523	PCR-SSCP	1,2
Bing-sheng Li	2016	China	Asian	HB	CRC	50	50	HRM	2
Nemati	2015	Iran	Caucasian	HB	CRC	202	203	PCR-SSCP	1,2
Omrane	2014	Tunis	Caucasian	PB	CRC	100	137	TaqMan	2
Omrane	2014	Tunis	Caucasian	PB	CRC	102	139	TaqMan	1
Xi	2015	China	Asian	HB	HCC	155	171	PCR-RFLP	1,2
Li	2014	China	Asian	HB	HCC	395	174	PCR-RFLP	1

Abbreviations: HB, hospital-based; PB, population-based; GC, gastric cancer; HCC, hepatocellular carcinoma; CRC, colorectal cancer. No. of SNP: No. 1, IL-17A rs2275913; No. 2, IL-17F rs763780.

CRC; (2) case-control design; and (3) available genotype and allele frequencies.

The exclusion criteria were as follows: (1) studies that did not investigate the relationship between the two polymorphisms and risk of digestive system neoplasms; (2) studies with a non-case-control design; (3) reviews, conference papers and abstracts; (4) repeated publications or the same studies appearing in different databases; and (5) studies that did not provide complete genotype and allele frequencies.

The data extraction was performed as follows: Two authors independently extracted the data from each study. When the opinions were inconsistent, a third person assisted in reaching a resolution. For each included study, the following information was obtained: first

Table 2
IL-17A rs2275913 and IL-17F rs763780 polymorphisms genotype distribution and allele frequency in cases and controls.

First author (year)	Genotype (case/control)			Allele frequency (case/control)		*H. pylori*	HWE
	AA	AB	BB	A	B		
IL-17A rs2275913							
Zhao (2016)	51/95	76/94	26/18	216/291	90/123	No	Yes
Yang (2016)	200/203	128/123	58/48	528/529	244/219	No	No
Qi (2015)	100/122	110/105	42/25	356/349	148/155	Yes	Yes
Hou and Yang (2015)	121/161	149/136	56/29	461/452	191/200	Yes	Yes
Gao (2015)	239/260	250/241	83/72	728/761	416/385	No	Yes
Gao Wei (2015)	200/203	128/123	58/48	528/529	244/219	No	Yes
Zhang (2014)	110/258	102/187	48/67	212/445	150/254	Yes	Yes
Gonzalez-Hormazabal (2014)	103/105	36/59	8/8	242/269	52/75	No	Yes
Wang (2014)	160/214	211/190	91/58	531/618	393/306	Yes	Yes
Zhu (2014)	126/273	122/216	45/61	374/762	212/338	Yes	Yes
Lan-qing Bi (2014)	32/41	39/69	28/40	103/151	95/149	No	Yes
Rafiei (2013)	56/78	61/72	44/21	173/228	149/114	No	Yes
Arisawa (2012)	112/218	137/293	84/72	361/729	305/437	No	Yes
Wu (2010)	210/193	485/371	250/204	905/757	985/779	No	Yes
Luo (2010)	11/58	12/126	1/46	34/242	14/218	Yes	Yes
Jian-jian Chen (2010)	300/325	522/541	220/224	1122/1191	962/989	Yes	Yes
Shibata (2009)	94/175	124/299	69/49	312/649	262/397	No	No
Nemati (2015)	100/110	82/50	20/39	282/270	122/128	–	No
Omrane (2014)	48/95	51/38	3/6	147/228	57/50	–	Yes
Xi (2015)	38/35	71/90	46/46	147/160	163/182	–	Yes
Li (2014)	110/50	197/85	84/39	417/185	365/163	–	Yes
IL-17 F rs763780							
Zhao (2016)	114/165	29/37	10/5	277/367	29/47	No	Yes
Yang (2016)	294/312	58/54	34/8	648/678	126/70	No	Yes
Qi (2015)	203/213	29/26	20/13	457/452	47/52	Yes	No
Hou and Yang (2015)	266/278	38/33	22/15	591/589	61/63	Yes	No
Gao (2015)	420/472	67/58	85/42	907/1002	237/142	No	Yes
Gao Wei (2015)	294/312	58/54	34/8	646/678	126/70	No	Yes
Wang (2014)	349/362	98/90	15/10	796/814	128/110	No	Yes
Zhu (2014)	241/463	35/58	17/29	517/984	69/116	No	Yes
Zhang (2014)	209/429	30/53	21/30	448/911	72/113	No	No
Gonzalez-Hormazabal (2014)	136/160	11/12	0/0	283/332	11/12	No	Yes
Lan-qing Bi (2014)	69/108	22/35	9/7	160/251	40/49	No	Yes
Wu (2010)	540/527	332/214	55/36	1412/1268	442/286	No	No
Luo (2010)	14/176	10/51	0/3	38/403	10/57	Yes	Yes
Shibata (2009)	221/419	55/100	4/4	497/938	63/108	No	Yes
Bing-sheng Li (2016)	37/40	13/10	0/0	87/90	13/10	–	Yes
Nemati (2015)	177/190	23/11	0/0	377/391	23/11	–	Yes
Omrane (2014)	72/98	27/38	1/1	171/234	29/40	–	Yes
Xi (2015)	100/105	46/63	9/3	246/273	64/69	–	Yes

A represents the major allele, B represents the minor allele. Abbreviations: HWE, Hardy-Weinberg equilibrium.

author's name, year of publication, ethnicity, sample size, cancer type, source of controls, genotyping method, genotype and allele frequencies in each case-control study, *H. pylori* infection status and *P*-value of Hardy-Weinberg equilibrium (HWE).

2.3. Statistical analysis

Statistical analysis was performed by Stata 11.0 software, where $P < 0.05$ showed statistical significance. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to assess the associations between the IL-17A rs2275913 and IL-17F rs763780 polymorphisms and susceptibility to digestive system neoplasms. Four major genetic models were selected for the meta-analysis: the allele model, the dominant model, the recessive model and the codominant model. Subgroup analyses were assessed by the cancer type, ethnicity, source of controls and *H. pylori* infection status. Heterogeneity was evaluated by *Q* test and I^2 test: if $P \geq 0.1$ and $I^2 \leq 50\%$, a fixed-effects model was selected; otherwise, a random-effects model was used. A sensitivity analysis evaluated the stability of the results by excluding each study sequentially. In addition, possible publication bias was evaluated by Begg's funnel plot and Egger's test. The *P*-value of HWE was obtained from the eligible studies.

3. Results

3.1. Characteristics of included literature

In all, 23 studies were included in our final meta-analysis to assess the associations between the IL-17A rs2275913 and IL-17F rs763780 polymorphisms and the risk of digestive system neoplasms. The specific process of the literature search is shown in Fig. 1. Among these, 21 studies [5–25] with 6789 cases and 8000 controls focused on the IL-17A rs2275913 polymorphism, while 18 studies [5,15,18,19,21,22,24,26,27], including 5073 cases and 6040 controls, focused on IL-17F rs763780. The specific characteristics of the eligible studies are shown in Table 1. The distribution frequencies of all genotypes and alleles are presented in Table 2.

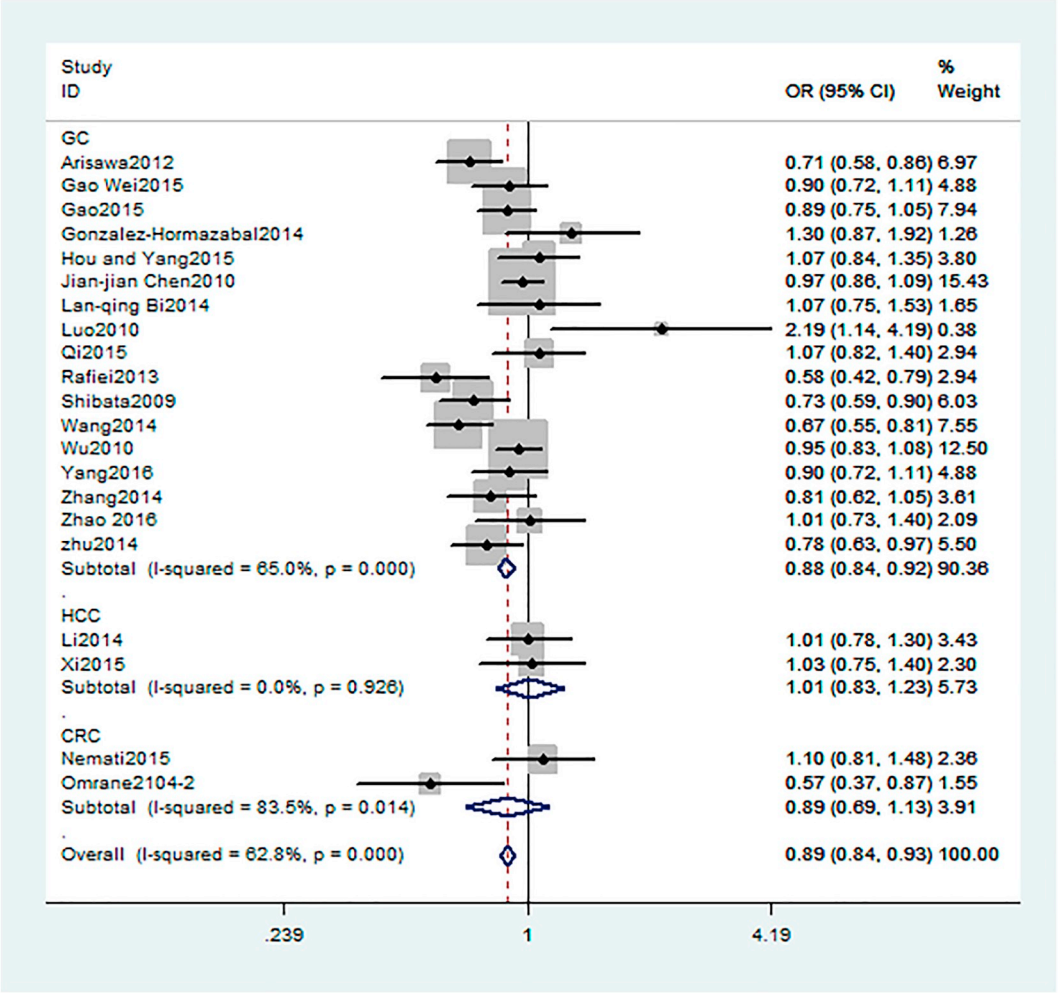

Fig. 2. Forest plot of IL-17A rs2275913 polymorphism and the risk of digestive system cancers in the allele model (A VS G).

3.2. Meta-analysis

3.2.1. IL-17A rs2275913 polymorphism

Overall, the results of the four genetic models were statistically significant ($P < 0.05$), which suggests that the IL-17A rs2275913 polymorphism was associated with susceptibility to cancers of the digestive system: allele model A VS G: OR = 0.89, 95% CI = 0.84–0.93 (Fig. 2); dominant model AA + AG VS GG: OR = 0.77, 95% CI = 0.70–0.84 (Fig. 3); recessive model GG + GA VS AA: OR = 1.21, 95% CI = 1.13–1.29 (Fig. 4); codominant model AA VS GG group: OR = 0.71, 95% CI = 0.65–0.79, AG VS GG group: OR = 0.81, 95% CI = 0.73–0.88. After eliminating studies that did not meet HWE, similar results were observed. The results are presented in Table 3.

Further subgroup analysis was conducted based on cancer type, and a significant association was found between the IL-17A rs2275913 polymorphism and susceptibility to GC in all genetic models: allele model A VS G: OR = 0.88, 95% CI = 0.84–0.92; dominant model AA + AG VS GG: OR = 0.73, 95% CI = 0.66–0.80; recessive model GG + GA VS AA: OR = 1.20, 95% CI = 1.12–1.29; codominant model AA VS GG group: OR = 0.68, 95% CI = 0.61–0.75, AG VS GG group: OR = 0.76, 95% CI = 0.69–0.84; however, no correlation was found between these polymorphisms and HCC or CRC. When subgroup analysis was performed according to ethnicity, IL-17 rs2275913 was significantly associated with the risk of digestive system neoplasms in Asian populations but not in Caucasians. When the results were classified according to the sources of the controls, IL-17A rs2275913 was associated with susceptibility to cancers of the digestive system in both hospital-based and population-based controls. *H. pylori* infection plays an important role in the development of GC, and thus the subgroup analysis was designed based on whether *H. pylori* infection was present in the GC cases. Associations were observed in both groups, and all comparisons are summarized in Table 3.

3.2.2. IL-17F rs763780 polymorphism

Overall, our quantitative analysis showed a strong association between the IL-17F rs763780 polymorphism and the risk of digestive system neoplasms in all genetic models: allele model T VS C: OR = 0.74, 95% CI = 0.69–0.80 (Fig. 5); dominant model TT + TC VS CC: OR = 0.53, 95% CI = 0.44–0.64 (Fig. 6); recessive model CC + TC VS TT: OR = 1.36, 95% CI = 1.24–1.49 (Fig. 7); and codominant model TT VS CC group: OR = 0.51, 95% CI = 0.43–0.61, TC VS CC group: OR = 0.63, 95% CI = 0.51–0.78. After removing the studies that deviated from HWE, we also observed consistent results in all genotype models (Table 3).

A subgroup analysis was also performed according to cancer type, ethnicity, sources of controls and *H. pylori* infection in GC. Expect for *H.*

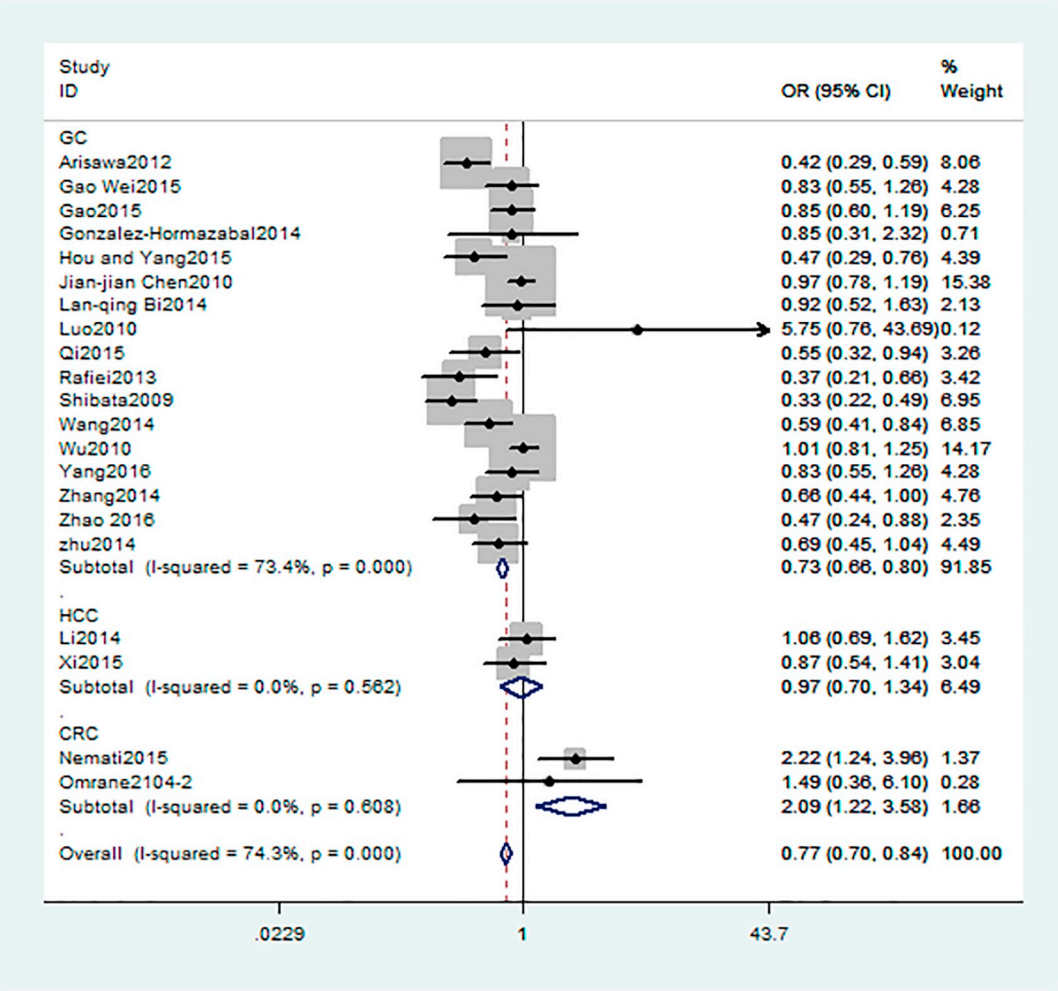

Fig. 3. Forest plot of IL-17A rs2275913 polymorphism and the risk of digestive system cancers using the dominant model (AA + AG VS GG).

pylori infection, we observed similar results for the IL-17A rs2275913 polymorphism. A significant association was found between the IL-17F rs763780 polymorphism and the risk of GC: allele model T VS C: OR = 0.74, 95% CI = 0.67–0.80; dominant model TT + TC VS CC: OR = 0.54, 95% CI = 0.45–0.65; recessive model CC + TC VS TT: OR = 1.39, 95% CI = 1.26–1.53; codominant model TT VS CC group: OR = 0.52, 95% CI = 0.43–0.62, TC VS CC group: OR = 0.65, 95% CI = 0.52–0.80. When the analysis was based on *H. pylori* infection status, the IL-17F rs763780 polymorphism was observed to be associated with the risk of GC in the *H. pylori*-negative group but not in the *H. pylori*-positive group (Table 3).

3.3. Heterogeneity and sensitivity analysis

Overall, significant heterogeneities were found in the data of the IL-17A rs2275913 polymorphism in all genetic models, even in the subgroup analysis. However, for the IL-17F rs763780 polymorphism, heterogeneity was only found in the allele model. Moreover, the subgroup analysis results were consistent with the overall results. Sensitivity analysis was performed to supplement the determination of sources of heterogeneity as well as to sequentially remove individual studies from all the analyses. The results showed that the overall OR with 95% CI did not change significantly, which indicates that the overall results were stable (Fig. 8).

3.4. Publication bias

Publication bias of the included articles was assessed by Begg's funnel plot and Egger's test. The funnel plots were symmetrical in shape, and a $P > 0.05$ for bias in Egger's test did not indicate publication bias for the IL-17A rs2275913 and IL-17F rs763780 polymorphisms (Figs. 9 and 10).

4. Discussion

IL-17 is a critical cytokine family that was originally determined to be secreted by Th17 cells [28]. Among the various family members, IL-17A and IL-17F play an important part in inflammation, autoimmune diseases and cancers [29,30]. In recent years, numerous studies have shown that polymorphisms in IL-17A and IL-17F can regulate transcription and translation, as well as further affect carcinogenesis [31,32]. Previous case-control studies have demonstrated associations between the IL-17A rs2275913 and IL-17F rs763780 polymorphisms and the susceptibility of digestive system neoplasms, especially gastric

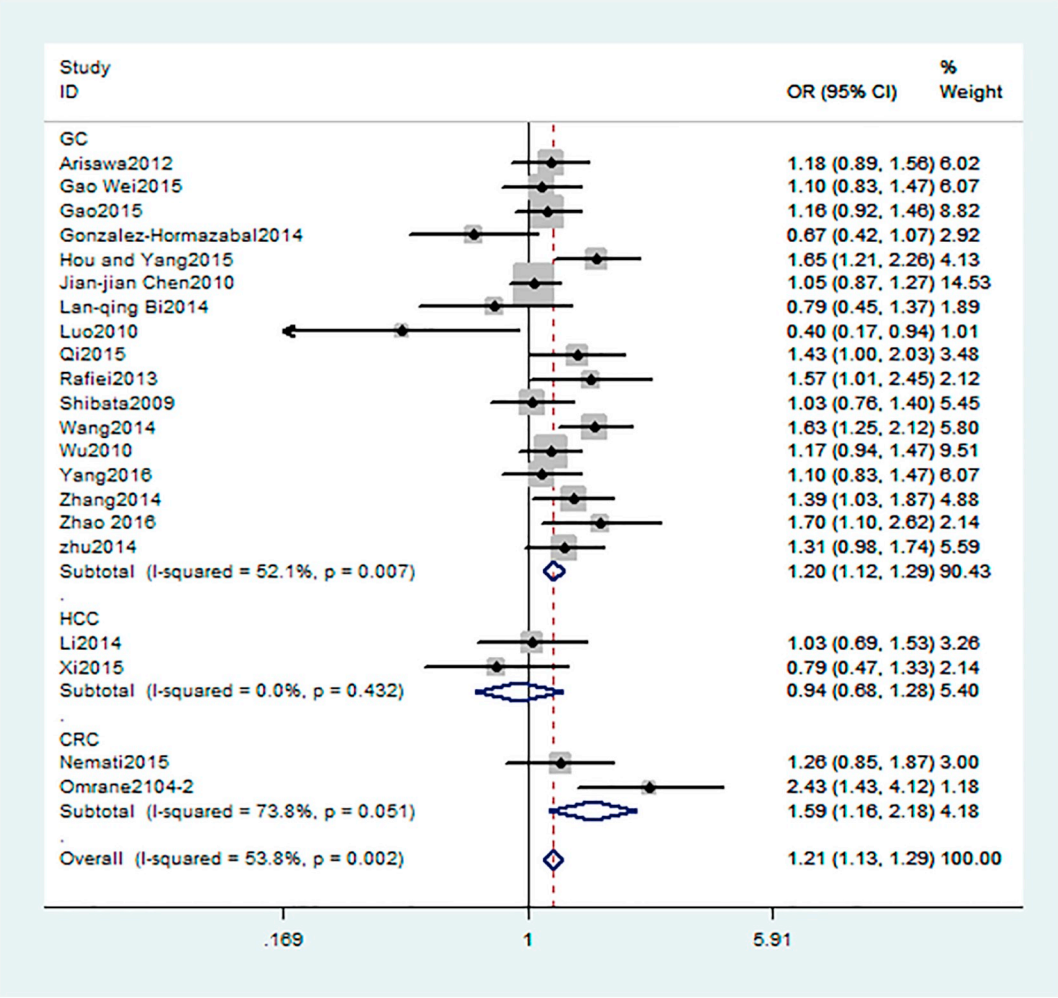

Fig. 4. Forest plot of IL-17A rs2275913 polymorphism and the risk of digestive system cancers in the recessive model (GG + GA VS AA).

cancer. However, these results were inconsistent because of differences in ethnicity, sample size, and source of controls, among other factors.

A meta-analysis was used to assess the associations between the two variants of the IL-17 family and susceptibility to cancers of the digestive system such as gastric cancer, hepatocellular carcinoma and colorectal cancer. Twenty-three case-control studies were included, of which 21 articles with 6978 cases and 8000 controls focused on IL-17A rs2275913, while 18 studies including 5073 cases and 6040 controls focused on IL-17F rs763780. Our results showed that both mutations were significantly associated with susceptibility to digestive system neoplasms in all genetic models, which remained consistent after the omission of studies that did not meet HWE. While subgroup analysis was performed in term of cancer type, IL-17A rs2275913 and IL-17F rs763780 polymorphisms were found to be significantly associated with the risk of gastric cancer but not with hepatocellular carcinoma or colorectal cancer; however, the sample size of those cancers was small. We also observed similar associations in Asian populations but not in Caucasian populations after stratifying by ethnicity. When the subgroup analyses were designed according to the source of controls, the two polymorphisms were observed to be correlated with susceptibility to digestive system cancers in hospital-based and population-based controls. In the analysis of IL-17A rs2275913, individuals with the AA genotype had a lower risk of digestive system neoplasms, while individuals with the GG genotype had an increased risk, which suggests that AA was a protective genotype. At the same time, analysis of IL-17F rs763780 revealed that the TT genotype decreased the risk of digestive cancers compared with the TC or CC genotypes.

However, this meta-analysis still had many deficiencies. First, the two polymorphisms were connected with susceptibility to cancers of the digestive system in all genetic models, but most of the included studies focused on gastric cancer, while few articles investigated other cancers. Thus, further studies are needed to provide reliable evidence. Second, the obvious heterogeneities that were found in the analyses of IL-17A rs2275913 could not be eliminated when subgroup analyses were performed based on cancer type, ethnicity and source of controls. Third, all included studies assessed Asian or Caucasian populations, and thus analyses of other ethnic groups are lacking. Therefore, more reliable studies are needed to perform a comprehensive analysis. Fourth, we could not consider the influence of other factors, such as age, sex, and smoking and drinking status. Therefore, more high-quality studies with large samples sizes are still required in order to assess the relationship between the IL-17A rs2275913 and IL-17F rs763780 polymorphisms and the risk of digestive system cancers.

Table 3
Summary of the ORs with 95% CIs and heterogeneity between the two polymorphisms and risk of digestive system cancers.

Groups and subgroups	Comparison	IL-17A rs2275913				IL-17F rs763780			
		OR	95% CI	*P*-value	I^2 (%)	OR	95% CI	*P*-value	I^2 (%)
Total	A VS B	0.89	0.84–0.93	< 0.0001	63	0.74	0.69–0.80	0.004	54
	AA + AB VS BB	0.77	0.70–0.84	< 0.00001	74	0.53	0.44–0.64	0.17	25
	BB + BA VS AA	1.21	1.13–1.29	0.002	54	1.36	1.24–1.49	0.45	1
	AA VS BB	0.71	0.65–0.79	< 0.0001	69	0.51	0.43–0.61	0.26	18
	AB VS BB	0.81	0.73–0.88	< 0.00001	74	0.63	0.51–0.78	0.17	26
Cancer type									
GC	A VS B	0.88	0.84–0.92	< 0.0001	65	0.74	0.67–0.80	0.003	59
	AA + AB VS BB	0.73	0.66–0.80	< 0.00001	73	0.54	0.45–0.65	0.12	33
	BB + BA VS AA	1.20	1.12–1.29	0.007	52	1.39	1.26–1.53	0.67	0
	AA VS BB	0.68	0.61–0.75	< 0.0001	68	0.52	0.43–0.62	0.17	27
	AB VS BB	0.76	0.69–0.84	< 0.00001	71	0.65	0.52–0.80	0.16	29
CRC	A VS B	0.89	0.69–1.13	0.01	84	0.76	0.53–1.11	0.23	32
	AA+AB VS BB	2.09	1.22–3.58	0.61	0	0.73	0.04–11.78	–	–
	BB + BA VS AA	1.59	1.16–2.18	0.05	74	1.36	0.91–2.03	0.22	34
	AA VS BB	1.63	0.93–2.84	0.48	0	0.73	0.05–11.94	–	–
	AB VS BB	3.01	1.72–5.59	0.83	0	0.71	0.04–11.87	–	–
HCC	A VS B	1.01	0.83–1.23	0.93	0	0.97	0.66–1.42	–	–
	AA + AB VS BB	0.97	0.70–1.34	0.56	0	0.29	0.08–1.09	–	–
	BB + BA VS AA	0.94	0.68–1.28	0.43	0	0.87	0.56–1.37	–	–
	AA VS BB	1.05	0.71–1.55	0.88	0	0.32	0.08–1.21	–	–
	AB VS BB	0.94	0.67–1.32	0.38	0	0.24	0.06–0.95	–	–
Ethnicity									
Asian	A VS B	0.89	0.84–0.94	0.001	58	0.74	0.68–0.80	0.004	56
	AA + AB VS BB	0.76	0.69–0.83	< 0.00001	72	0.53	0.44–0.64	0.13	31
	BB + BA VS AA	1.20	1.11–1.29	0.02	45	1.36	1.24–1.49	0.52	0
	AA VS BB	0.71	0.64–0.78	< 0.0001	67	0.51	0.43–0.61	0.20	23
	AB VS BB	0.79	0.72–0.87	< 0.00001	70	0.63	0.51–9.78	0.13	31
Caucasian	A VS B	0.75	0.62–0.91	0.006	81	0.77	0.51–1.16	0.09	66
	AA + AB VS BB	0.93	0.65–1.35	< 0.0001	89	0.73	0.04–11.78	–	–
	BB + BA VS AA	1.59	1.23–2.05	0.15	48	1.35	0.86–2.10	0.08	67
	AA VS BB	0.82	0.55–1.21	0.0010	86	0.73	0.05–11.94	–	–
	AB VS BB	1.18	0.79–1.75	< 0.0001	91	0.71	0.04–11.87	–	–
HWE (Yes)	A VS B	0.89	0.85–0.94	< 0.0001	65	0.71	0.65–0.79	0.006	55
	AA + AB VS BB	0.78	0.71–0.85	0.0001	64	0.44	0.35–0.55	0.24	21
	BB + BA VS AA	1.22	1.13–1.32	0.0007	59	1.33	1.18–1.49	0.27	17
	AA VS BB	0.71	0.64–0.79	0.0001	64	0.43	0.34–0.54	0.26	19
	AB VS BB	0.82	0.75–0.90	0.003	53	0.49	0.38–0.65	0.32	13
Design									
HB	A VS B	0.89	0.83–0.95	0.003	58	0.75	0.68–0.84	0.002	63
	AA + AB VS BB	0.69	0.61–0.79	< 0.00001	76	0.49	0.39–0.62	0.35	10
	BB + BA VS AA	1.22	1.11–1.34	0.01	53	1.35	1.19–1.53	0.31	14
	AA VS BB	0.68	0.59–0.77	< 0.0001	71	0.48	0.38–0.61	0.38	7
	AB VS BB	0.72	0.63–0.82	< 0.0001	78	0.56	0.43–0.74	0.42	2
PB	A VS B	0.88	0.82–0.94	0.0010	73	0.73	0.65–0.82	0.22	29
	AA + AB VS BB	0.84	0.75–0.95	0.008	65	0.60	0.45–0.80	0.11	48
	BB + BA VS AA	1.19	1.08–1.32	0.02	62	1.37	1.20–1.57	0.51	0
	AA VS BB	0.76	0.66–0.87	0.007	66	0.56	0.42–0.74	0.15	40
	AB VS BB	0.90	0.79–1.02	0.07	49	0.73	0.54–1.01	0.09	50
H. pylori									
Positive	A VS B	0.90	0.83–0.97	0.0005	75	1.00	0.77–1.29	0.23	32
	AA + AB VS BB	0.76	0.66–0.87	0.010	64	0.65	0.40–1.06	0.99	0
	BB + BA VS AA	1.29	1.16–1.44	0.007	66	1.39	1.04–1.86	0.47	0
	AA VS BB	0.68	0.58–0.79	0.001	73	0.64	0.39–1.04	0.99	0
	AB VS BB	0.83	0.71–0.96	0.18	32	0.78	0.44–1.39	0.91	0
Negative	A VS B	0.86	0.81–0.92	0.01	58	0.71	0.65–0.77	0.010	57
	AA + AB VS BB	0.71	0.63–0.80	< 0.00001	79	0.52	0.43–0.64	0.04	48
	BB + BA VS AA	1.14	1.03–1.25	0.18	29	1.39	1.25–1.54	0.55	0
	AA VS BB	0.67	0.59–0.77	0.001	67	0.50	0.41–0.61	0.07	43
	AB VS BB	0.72	0.63–0.82	< 0.00001	80	0.63	0.50–0.79	0.06	45

Abbreviations: A represents the major allele, B represents the minor allele. Abbreviations: GC, gastric cancer; HCC, hepatocellular carcinoma; CRC, colorectal cancer; HB, hospital-based; PB, population-based; CI, confidence interval; OR, odds ratio.

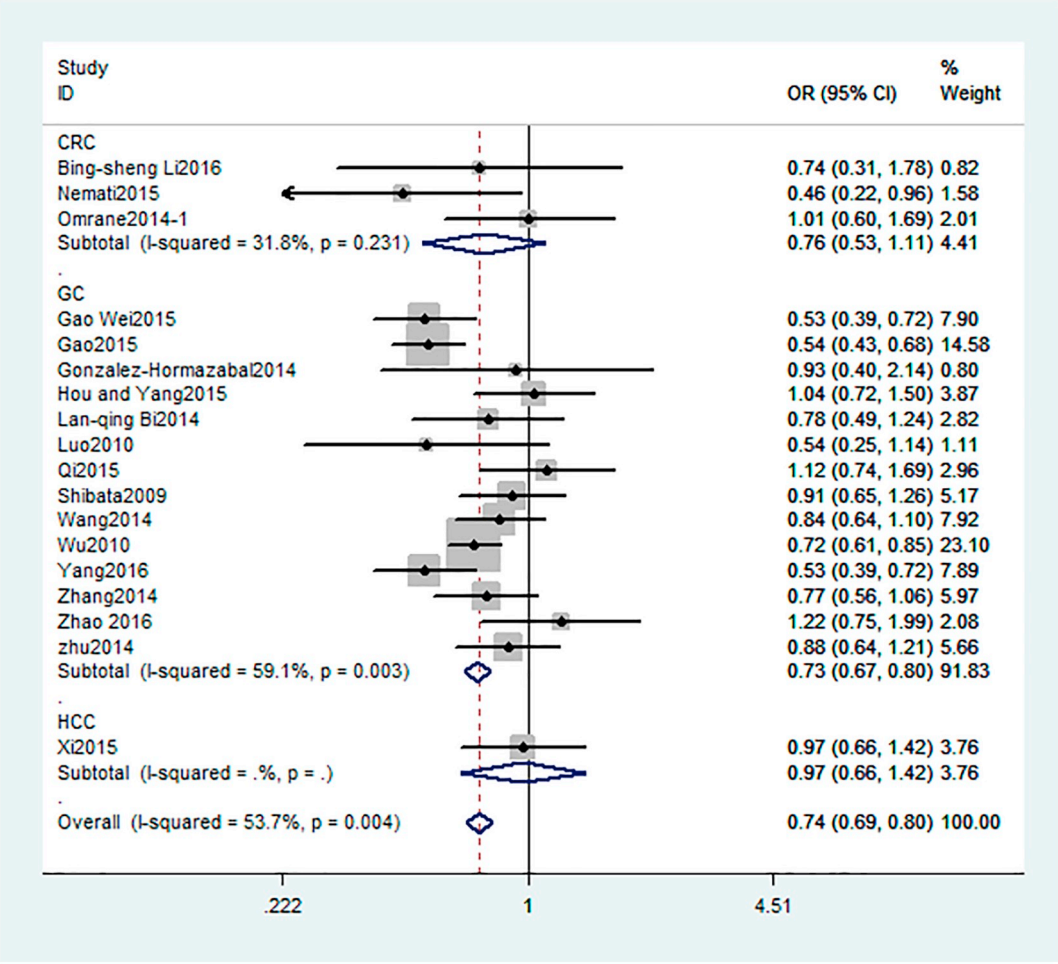

Fig. 5. Forest plot of IL-17F rs763780 polymorphism and the risk of digestive system cancers in the allele model (T VS C).

Competing interests

The authors declare that they have no competing interests.

Author's contribution

Jie-Fang Gao designed the study, analyzed the data and wrote the first daft. Hong Zhang proofread and revised the submission. Jian Lv directed the statistical analyses of the data. Li Wang and Yue-Ying Fan retrieved documents and extracted data. All authors contributed to the discussion and approved the final manuscript.

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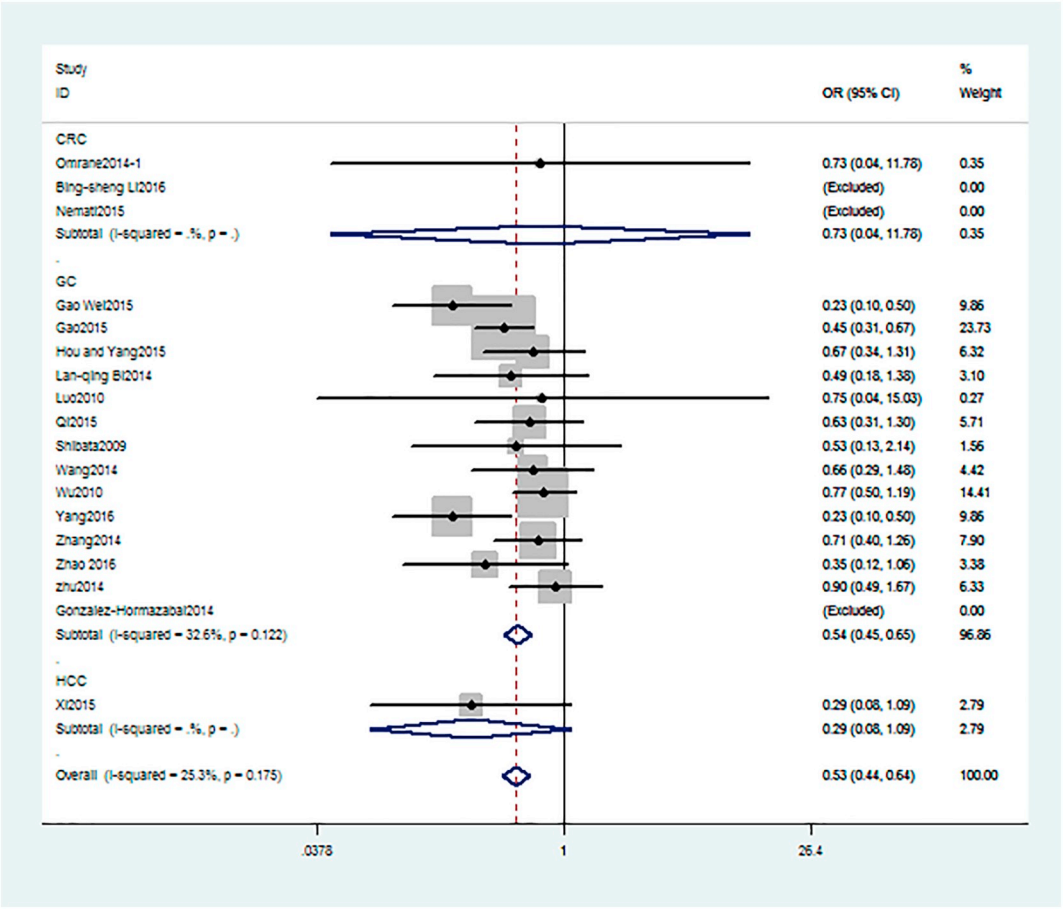

Fig. 6. Forest plot of IL-17F rs763780 polymorphism and the risk of digestive system cancers using the dominant model (TT + TC VS CC).

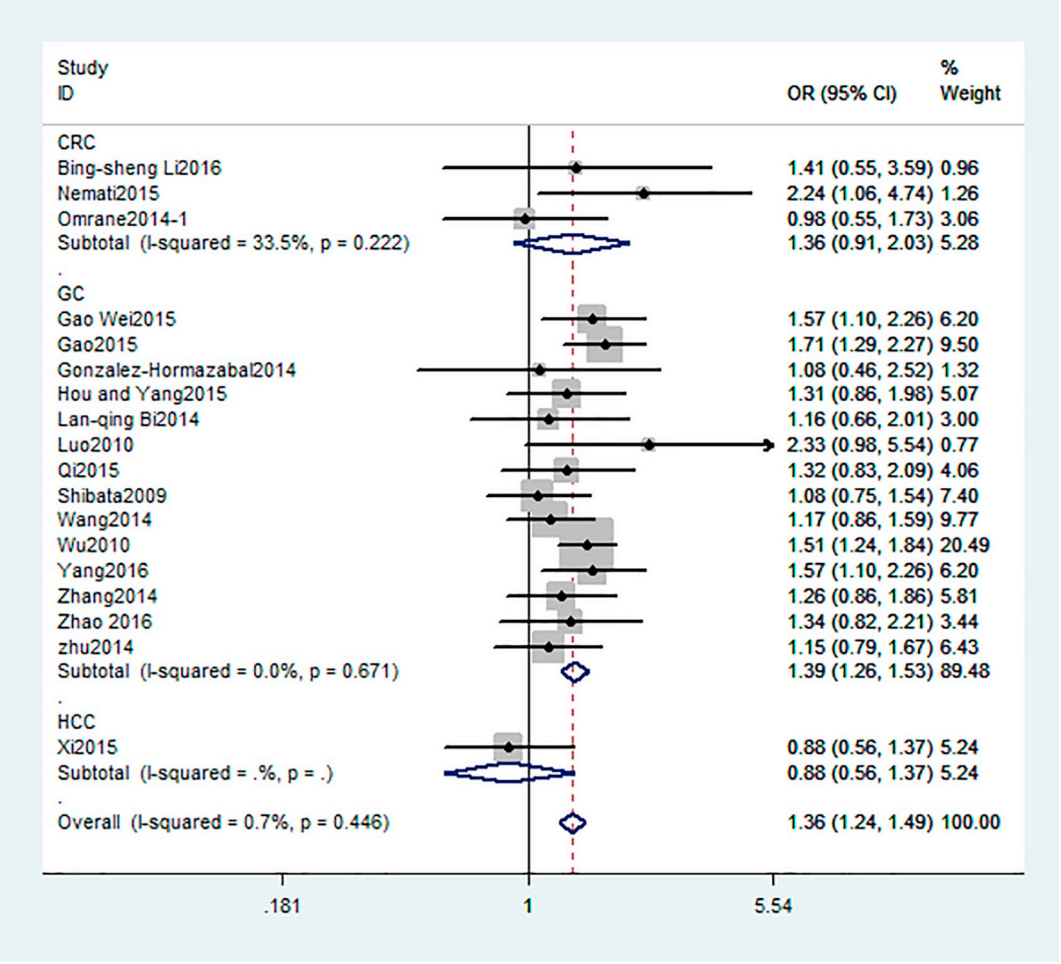

Fig. 7. Forest plot of IL-17F rs763780 polymorphism and the risk of digestive system cancers in the recessive model (CC + CT VS TT).

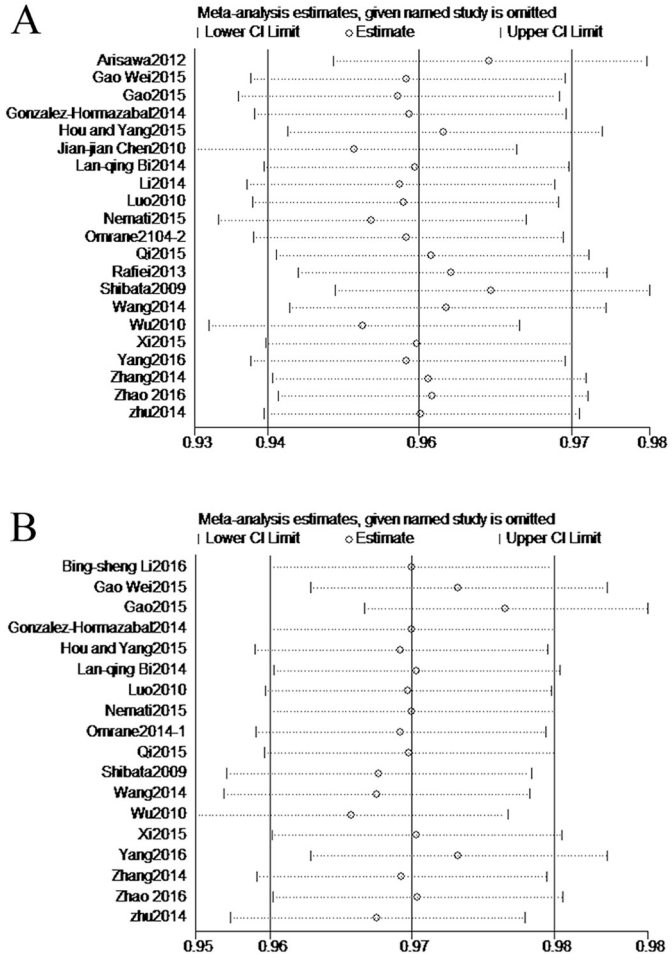

Fig. 8. Sensitivity analysis about the two polymorphisms and the risk of digestive system cancers in the dominant model. A, IL-17A rs2275913; B, IL-17F rs763780.

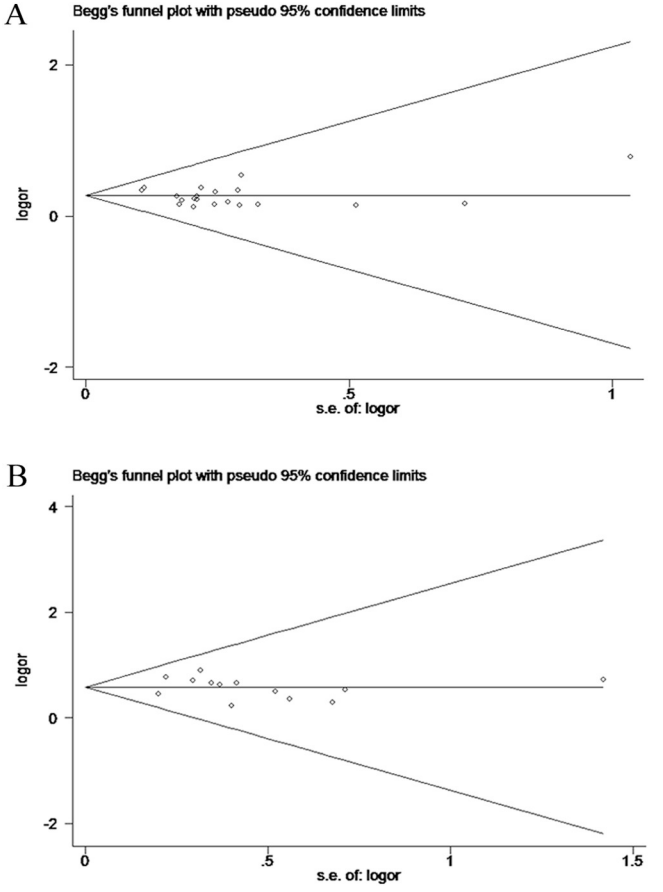

Fig. 9. Begg's funnel plots used to evaluate publication bias between the two polymorphisms and the risk of digestive system neoplasms in the dominant model. A, IL-17A rs2275913; B, IL-17F rs763780.

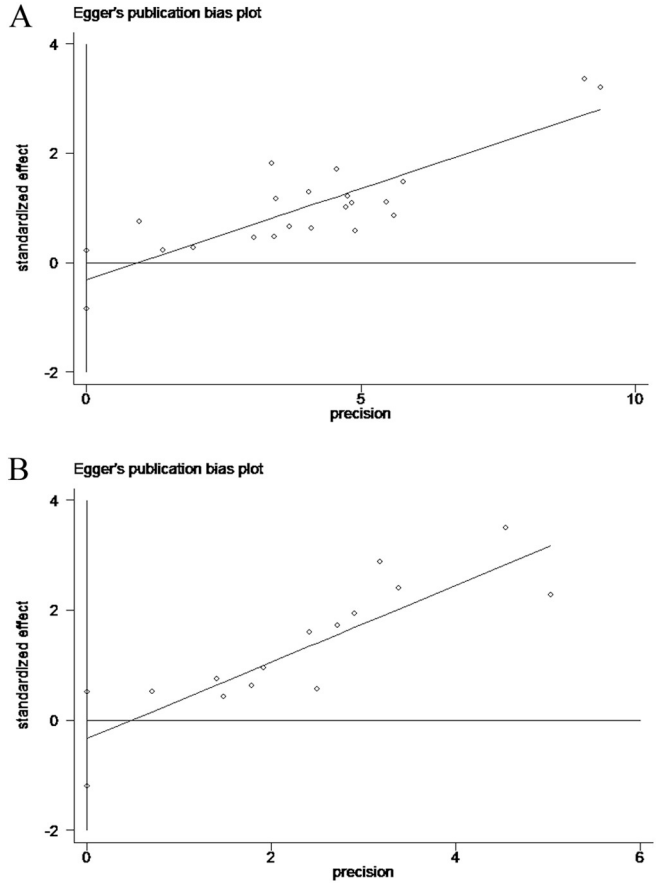

Fig. 10. Egger's test assessing evidence of publication bias for the dominant model of the two polymorphisms. A, IL-17A rs2275913; B, IL-17F rs763780.

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