publications up to May 2014. Then, we performed an updated meta-analysis that increases statistical power derive a more comprehensive and precise estimation of th relationship.

METHODS

Two investigators (Ji QS and Qi B) independently searche PubMed and EMBASE for eligible articles with the search strategy ("LOXL1" OR "Lysyl oxidase-like 1") and ("glaucoma" OR "exfoliation" OR "pseudoexfoliation"). We performed the final search on May 5, 2014.

We included only published manuscripts with English language restriction. All the studies have to fulfill the following criteria: 1) the studies reported on the associatio of three single nucleotide polymorphisms (SNPs) in LOXL1 (rs1048661, rs2165241, and/or rs3825942) polymorphism with XFS/XFG using either case-control or cohort design; 2) the studies must offer the sample size, distribution of alleles and/or genotype frequencies/counts in both patients and controls; 3) when multiple publications reported on the same or overlapping data, we used the most recent or largest population; and 4) if several different cohorts were reported in the same article, they were treated as independent studies. Exclusion criteria were: 1) studies with family-based designs; 2) studies on other gene polymorphism.

Two investigators (Ji QS and Qi B) independently extracted data and reached a consensus on all of the items. If there was disagreement in the retrieved information, a third reviewer (Liu L) would participate in the review. For each study, the following data were extracted: first author's surname, year of publication, ethnicity, sample size, allele, and/or genotype frequency/counts in both patients and controls.

The statistical analysis was performed by STATA statistical software (Version 12.0; STATA Corporation, College Station, TX, USA). We first examined whether the genotype distribution in controls of each study was consistent with Hardy-Weinberg equilibrium (HWE) by χ^2 test. The strength of the association between LOXL1 gene polymorphisms (rs1048661, rs2165241, and rs3825942) and susceptibility to XFS/XFG were estimated by ORs and 95% CIs. The pooled ORs were performed for allelic model, dominant model, recessive model, and additive model respectively. The significance of the pooled ORs was determined by Z test and P<0.05 was considered as statistically significant. Subgroup analysis was also performed by ethnicity. Heterogeneity among studies was assessed with the Q -test and I^2 statistics, P<0.10 and I^2 >50% indicated evidence of heterogeneity. Then, the random-effects model was used to calculate the pooled ORs. Otherwise, the fixed-effects model was applied. Sensitivity analysis was performed to examine the stability of the pooled effect after removing one study at a time. Publication bias was analyzed by performing funnel plots qualitatively, and estimated by Egger's test quantitatively. Two-sided P values <0.05 were considered statistically significant. In association analyses, the bonferroni correction was used to account for multiple testing[15]. Because four genetic models (allelic, dominant, recessive, and additive) were tested in three subgroups (Caucasians, Asians and Africans) for each SNP, a value of P<0.004 was considered statistically significant.

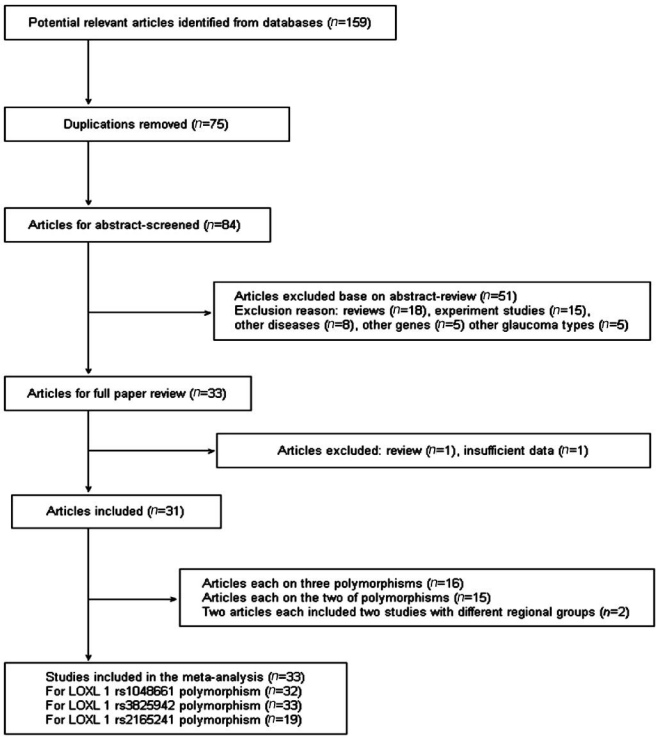

Figure 1 Flow diagram of the study selection for the Meta-analysis.

RESULTS

A number of 159 articles were preliminarily yielded from PubMed and EMBASE. After the abstract were screened and the full-text reviewed, a total of 33 studies were finally identified in 31 publications. The flow of study selection is shown in Figure 1, and the detailed study characteristics were summarized in Table 1. In the included studies, there were 21 groups of Caucasians, 10 groups of Asians, and 2 groups of Africans. The HWE of all three SNPs was calculated in the controls of all studies. No deviation from the HWE was identified. Combined analysis of the extracted datasets showed significant heterogeneity (P<0.00001, I^2>90%) among studies for three SNPs. However, no heterogeneity was observed in the subgroup analyses except studies of rs1048661 polymorphisms in Asians (P<0.0001, I^2=94%)

Table 1 Characteristics of publications included in meta-analysis of LOXL1 polymorphism and XFS/XFG

First Author	Year	Ethnicity	Country	Sample size		rs1048661G(%)		rs3825942G (%)		rs2165241T(%)	
				Case	Control	Case	Control	Case	Control	Case	Control
Thorleifsson *et al*[8]	2007	Caucasian	Iceland	130	14474	80.9	63.7	98.4	85.6	74.6	47.3
Thorleifsson *et al*[8]	2007	Caucasian	Sweden	199	198	83.4	68.2	99.5	87.8	81.3	53.5
Lemmela *et al*[9]	2009	Caucasian	Finland	141	404	82.5	68.3	96.8	82.3	73.2	46.8
Lee *et al*[10]	2009	Asian	China	62	171	52.4	44.4	99.2	91.8	NA	NA
Chen *et al*[11]	2009	Asian	China	50	124	11.0	48.4	100	89.6	2.0	10.0
Tanito *et al*[12]	2008	Asian	Japan	142	157	4.9	55.4	99.3	80.6	0.7	12.4
Ramprasad *et al*[13]	2008	Caucasian	India	52	97	72.1	63.4	92.3	74.2	NA	NA
Pasutto *et al*[16]	2008	Caucasian	Germany	517	348	81.8	63.9	95.1	83.5	75.2	47.9
Pasutto *et al*[16]	2008	Caucasian	Italy	209	70	82.5	69.3	100	82.1	79.8	50.7
Ozaki *et al*[17]	2008	Asian	Japan	209	172	5.3	49.7	98.6	86.3	1.7	10.2
Mossbock *et al*[18]	2008	Caucasian	Europe	167	170	84.1	67.1	99.4	81.8	NA	NA
Mori *et al*[19]	2008	Asian	Japan	95	190	0.5	47.4	99.5	85.3	NA	NA
Mabuchi *et al*[20]	2008	Asian	Japan	89	191	0.6	45.0	99.4	85.3	NA	NA
Hewitt *et al*[21]	2008	Caucasian	Australia	86	2087	77.9	66.0	94.8	84	NA	NA
Hayashi *et al*[22]	2008	Asian	Japan	59	190	0.8	46.0	100	85.7	NA	NA
Fuse *et al*[23]	2008	Asian	Japan	56	138	3.6	49.3	100	87.7	1.8	5.8
Fan *et al*[24]	2008	Caucasian	US	206	88	82.9	71.9	98.8	79.5	76.0	45.6
Challa *et al*[25]	2008	Caucasian	US	50	235	79.0	66.6	98.8	84.5	67.0	48.7
Aragon-Martin *et al*[26]	2008	Caucasian	Europe	287	333	84.3	70.3	96	79.8	73.4	44.8
Fingert *et al*[27]	2007	Caucasian	US	72	75	81.9	60.0	98.6	88	NA	NA
Wolf *et al*[28]	2010	Caucasian	Germany	128	280	84.4	66.0	99.2	85.6	78.2	49.1
Yang *et al*[29]	2008	Caucasian	US	62	170	NA	NA	100	85	83.1	52.1
Parkdo *et al*[30]	2013	Asian	Korean	110	127	2.7	29.5	91.1	89.8	1.0	6.5
Kasim *et al*[31]	2013	Caucasian	Turkey	200	100	87.5	71.0	100	84	NA	NA
Micheal *et al* I[32]	2012	Caucasian	Pakistani	128	180	85.2	65.8	97.3	83.9	NA	NA
Jaimes *et al*[33]	2012	Caucasian	Mexica	102	97	78.9	80.4	100	95.4	71.1	50.5
Sagong *et al*[34]	2011	Asian	Korean	89	146	7.3	35.6	98.3	89.4	1.7	9.2
Rautenbach *et al*[35]	2011	African	South Africa	43	47	100	88.3	14.3	61.7	NA	NA
Mayinu *et al*[36]	2011	Caucasian	Uygur	64	127	81.3	69.3	95.3	80.7	56.3	24.4
Malukiewicz *et al*[37]	2011	Caucasian	Poland	36	30	90.3	80.0	100	86.7	NA	NA
Fan *et al*[38]	2011	Caucasian	US	196	201	84.7	72.9	99.2	81.1	78.3	47.0
Williams *et al*[39]	2010	African	South africa	50	50	99.0	81.0	13	62	NA	NA
Abu-Amero *et al*[40]	2010	Caucasian	Saudi Arabia	93	101	87.6	76.2	96.8	81.7	NA	NA

NA: Not applicable.

and rs3825942 polymorphisms in Caucasians (P<0.0001, I^2=66%).

For rs1048661 polymorphism, a total of 4081 cases and 7834 controls were included in 32 studies. Overall, the results showed that no significant association between this polymorphism and XFS/XFG risk was observed in all genetic models (G *vs* T: OR=0.91, 95% CI=0.62-1.35, P=0.65; GG *vs* TT: OR= 1.29, 95% CI=0.57-2.92, P=0.54; GG/GT *vs* TT: OR= 0.81, 95% CI=0.32-2.06, P=0.56) and recessive model (GG *vs* GT/TT: OR= 1.54, 95% CI=1.14-2.10, P=0.006; Table 2). In subgroup analysis by ethnicity, the risk of developing XFS/XFG was remarkably increased in Caucasians (G *vs* T: OR= 2.19, 95% CI=1.96-2.45, P<0.00001) and Africans (G *vs* T: OR= 23.42, 95% CI=4.48-122.52, P=0.0002) and significantly decreased in Asians (G *vs* T: OR= 0.06, 95% CI=0.02-0.18, P<0.00001; Figure 2).

For rs3825942 polymorphism, 33 studies consisting of 4147 cases and 7488 controls were obtained. The overall data under any genetic models (G *vs* A: OR=9.21, 95% CI=5.12-16.54, P <0.00001; GG *vs* AA: OR= 5.81, 95% CI=2.67- 12.67, P <0.00001; GG/GA *vs* AA: OR= 8.13, 95% CI=1.92-1.76, P =8.88, P =0.0003; GG *vs* GA/AA: OR=11.42, 95% CI=7.23-18.04, P <0.00001) indicated that the G allele of rs3825942 had increased risk of XFS/XFG compared to the T allele (Table 2). In subgroup analyses, the G allele was found to confer an increase risk for XFS/XFG among Caucasians (OR=8.80, 95% CI=6.05-12.79, P<0.00001) and Asians (OR= 14.92, 95% CI=9.15-24.34, P<0.00001). However, the G allele of rs3825942 have been investigated as a protective factor for XFS/XFG among Africans (OR= 0.09, 95% CI=0.06-0.15, P=0.0002) (Figure 3).

For rs2165241 polymorphism, 19 studies including 2889 cases and 17762 controls were investigated. The overall results suggested that the rs3825942 polymorphisms was association with XFS/XFG risk (T *vs* C: OR=1.94, 95% CI=1.44-2.61, P <0.00001; TT *vs* CC: OR=9.85, 95% CI=6.72-14.43, P<0.00001; TT/TC *vs* CC: OR=2.12, 95% CI=1.09-4.12, P <0.03; TT *vs* TC/CC: OR=4.28, 95%

Table 2 Stratification analyses of XFS/XFG susceptibility associated with LOXL1 polymorphisms

SNP	Ethnicity	Study	Genetic contrast		Study	Genetic contrast		Genetic contrast		Genetic contrast	
rs1048661											
		n	G *vs* T		*n*	GG *vs* TT		GG/GT *vs* TT		GG *vs* GT/TT	
			OR (95% CI)	I^2 (%)		OR(95% CI)	I^2 (%)	OR (95% CI)	I^2 (%)	OR (95% CI)	I^2 (%)
	Total	32	0.91 (0.62,1.35)	95	27	1.29 (0.57,2.92)	90	0.81 (0.32, 2.06)	95	1.54 (1.14,2.10)	83
	Caucasian	20	2.19 (1.96,2.45)	32	17	5.36 (3.81,7.53)	24	3.90 (2.79, 5.45)	24	2.51 (2.15, 2.94)	43
	Asian	10	0.06 (0.02,0.18)	94	9	0.05 (0.01,0.23)	89	0.03 (0.01,0.11)	93	0.12 (0.03,0.49)	87
	African	2	23.42 (4.48,122.52)	0	1	3.48 (0.14,88.00)	NA	2.81 (0.11,70.75)	NA	24.36(1.38,429.83)	NA
rs3825942											
	Varibles	*n*	G *vs* A		*n*	GG *vs* AA		GG/GA *vs* AA		GG *vs* GA/AA	
			OR (95% CI)	I^2 (%)		OR (95% CI)	I^2 (%)	OR (95% CI)	I^2 (%)	OR (95% CI)	I^2 (%)
	Total	33	9.21 (5.12,16.54)	90	27	5.81 (2.67,12.67)	59	4.13 (1.92,8.88)	67	11.42 (7.23,18.04)	74
	Caucasian	21	8.80 (6.05,12.79)	66	17	8.79 (5.04,15.33)	0	5.07 (3.29,7.82)	0	10.57 (6.96, 16.06)	63
	Asian	10	14.92 (9.15,24.34)	0	9	4.94 (1.60,15.24)	0	3.79 (1.23,11.68)	0	18.74 (10.26,34.24)	0
	African	2	0.09 (0.06,0.15)	NA	1	0.06 (0.02,0.20)	NA	0.04 (0.01,0.12)	NA	0.19 (0.06,0.58)	NA
rs2165241											
	Varibles	*n*	T *vs* C		*n*	TT *vs* CC		TT/TC *vs* CC		TT *vs* TC/CC	
			OR (95% CI)	I^2 (%)		OR (95% CI)	I^2 (%)	OR (95% CI)	I^2 (%)	OR (95% CI)	I^2 (%)
	Total	19	1.94 (1.44,2.61)	89	15	9.85 (6.72,14.43)	57	2.12 (1.09,4.12)	90	4.28 (3.65,5.03)	19
	Caucasian	13	3.41 (3.11,3.73)	0	10	10.69 (8.50,13.4)	0	5.72 (4.56,7.18)	11	4.39 (3.83, 5.05)	0
	Asian	6	0.15 (0.09,0.25)	0	5	0.26 (0.04,1.56)	0	0.13 (0.07,0.25)	0	0.31 (0.05,1.85)	0

P value of Z-test for overall effect; NA: Not applicable; I^2 statistics for heterogeneity test.

CI=3.65-5.03, *P* <0.00001; Table 2). In stratification analyses by ethnicity, the T allele of rs3825942 have been showed as risk factors for XFS/XFG in Caucasians (OR=3.41, 95% CI=3.11-3.73, *P*<0.00001). On the contrary, the lower risk of XFS/XFG was found in Asians (OR=0.15, 95% CI=0.09-0.25, *P*<0.00001; Figure 4).

Sensitivity analyses were carried out to assess the influence of each individual study on the pooled ORs by omitting one single study each time. The results showed that no individual study remarkable affected the pooled ORs, thus indicating that the results of this meta-analysis are stable.

Publication bias was firstly examined by Begg's funnel plot and estimated by Egger's tests quantitatively. In the overall analyses, the results suggested obvious evidence of publication bias for rs1048661 and rs3825942 (*t*=3.2, *P*=0.003 and *t*=2.6, *P*=0.014, respectively), while for rs2165241, the funnel plots was symmetrical (*t*=0.69, *P*=0.503; Figure 5A-C). In the subgroup analyses, Neither Begg's funnel plot nor Egger's test detected obvious evidence of publication bias in Caucasians and Asians (All *P* >0.05), except for rs3825942 in Caucasians (*t*=5.17, *P*=0.000) (data did not show).

DISCUSSION

The present Meta-analysis, consisting of 33 studies, investigated the three polymorphisms (rs1048661, rs3825942, and rs2165241) in LOXL1 gene and their associations with XFS/XFG risk. On the whole, the results showed that significantly increased XFS/XFG risk were found in all subjects with two polymorphisms (rs3825942 and rs2165241) within the LOXL1 gene under any genetic models. No significant correlation was found between LOXL1 rs1048661 polymorphism and XFS/XFG risk. Because the allele frequencies and distribution of three polymorphisms (rs1048661, rs3825942, and rs2165241) were diverse in the different ethnicities, we carried out stratified analysis by ethnicity. The results pointed to an increased risk of XFS/XFG among Caucasians with rs1048661 G and rs2165241 T allele (OR=2.19 and 3.41, respectively). In contrast, the two alleles showed a protective factor for XFS/XFG among Asians, with an OR 0.06 and 0.15, respectively, while the G allele of rs3825942 play a risk role in Caucasians and Asians (OR=9.21, and OR=14.92, respectively). A protective effect of rs3825942 G allele and risk effect of rs1048661 G allele were found in Africans with

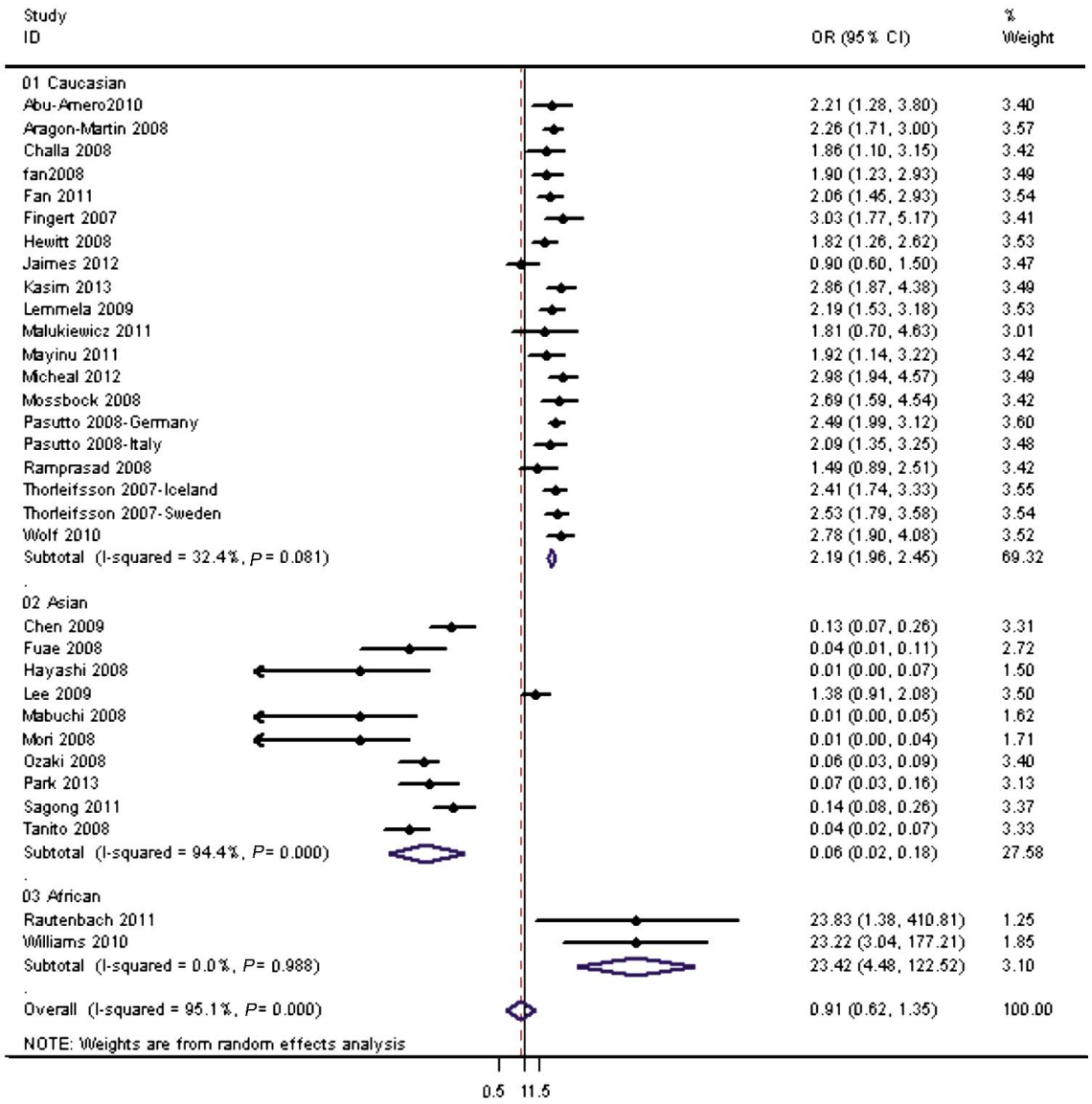

Figure 2 Forest plot from the meta-analysis of single nucleotide polymorphism (SNP) rs1048661 and risk of XFS/XFG in allelic risk model (G *vs* T) for different ethnicities.

two studies. Since limited Studies were from Africans, it is critical that larger studies based on Africans should be performed to re-evaluate the association.

Previous Meta-analysis showed that the genetic effect of rs3825942 is similar in different populations (Caucasian, Japanese, Chinese and Indian)[38]. However, there was inconsistence in the effect of rs1048661 and rs2165241 between Chinese and Japanese populations. Given the small size of subjects, we performed a combined analysis of Chinese, Japanese and Korean populations as Asians. The results indicated that the two polymorphisms (rs1048661 and rs3825942) of LOXL1 gene were correlated with XFS/XFG in Asians. The data may be more convincible due to the much larger number of the included studies. Nevertheless, considering the ethnicity-specific polymorphisms with XFS/XFG, more investigations with large sample sizes are required to detect the association among different groups.

The LOXL1 gene is a member of the lysyl oxidase family, which is necessary for the formation and maintenance of elastic tissue, playing an important role in the homeostasis of the extracellular matrix by inducing cross-linking in collagen and elastin molecules[41]. Thus, any alteration of LOXL1 activation, processing, and or substrate specificity may influence the function, synthesis, and subsequent deposition of the extracellular tissues. It has been reported in a recent study that reduced expression levels of LOXL1 and elastic proteins in the lamina cribrosa can increase the risk of pseudoexfoliation syndrome[42]. However, the causative functional role of LOXL1 polymorphisms played in the pathogenesis of XFS/XFG remains unclear. Neither rs1048661 nor rs3825942 polymorphism have been found to affect LOXL1 expression levels. In our Meta-analysis, we detected discrepancies in the effect of rs1048661 and rs2165241 polymorphisms between Caucasians and Asians.

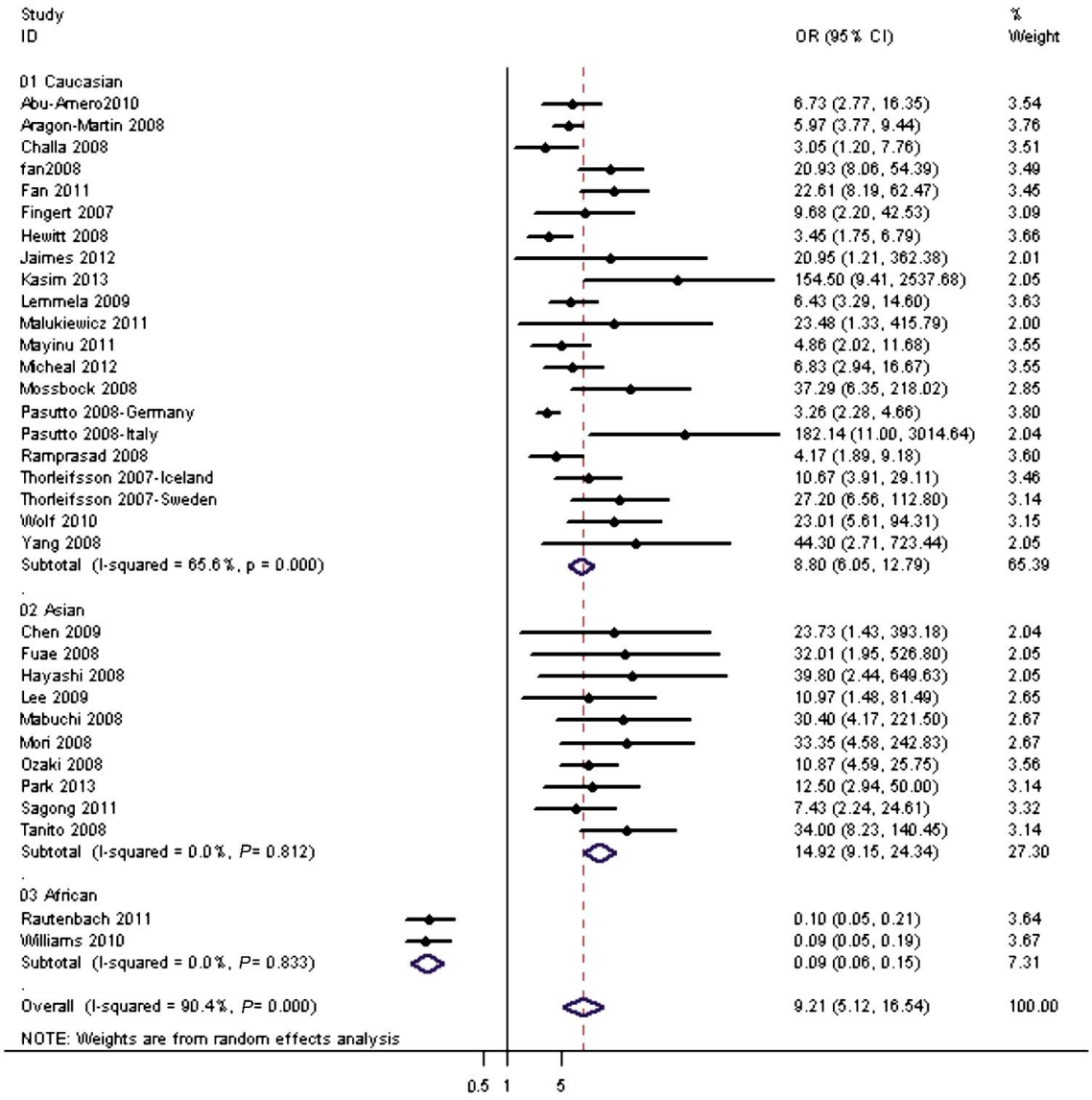

Figure 3 Forest plot from the Meta-analysis of single nucleotide polymorphism (SNP) rs3825942 and risk of XFS/XFG in allelic risk model (G *vs* A) for different ethnicities.

These inconsistencies in genetic findings among different ethnic groups suggest that missense changes in these SNPs of LOXL1 are not directly responsible for the development of XFS/XFG, while other unidentified genetic or environmental factors may affect LOXL1 gene expression or protein function, which needs further investigation.

Some limitations of this Meta-analysis should be addressed. First, only published studies were identified, while unpublished data and articles published in languages other than English were missed, which may have biased our results, although no obvious publication bias was apparent. Second, the controls were recruited in different ways and not uniformly defined, which may have distorted the Meta-analysis. Third, XFS/XFG is an age-related complex disease that results of combined effects of multifactor, including genetic and environmental factors. As none of the studies included in this meta-analysis considered the effect of gene-gene and environment interactions involved in the pathogenesis of XFS/XFG, this issue could not addressed in our Meta-analysis. Fourth, ethnicity was determined by populations' country due to inadequate available data. Furthermore, only Caucasians, Asians and Africans were concerned in the subgroup analysis. Thus, data regarding other ethnicity are desired. Fifth, adjustments over age, gender might help better detect the association between LOXL1 and XFS/XFG risk. Sixth, as is known, haplotype analysis might bring out bigger net effects. However, most studies did not perform haplotype analyses, which hampered our further analysis. Finally, all the studies were designed with retrospective studies. We cannot clearly determine the relationship between the LOXL1 polymorphisms and XFS/XFG risk.

In summary, our Meta-analyses suggested that the three LOXL1 polymorphisms (rs1048661, rs3825942, and

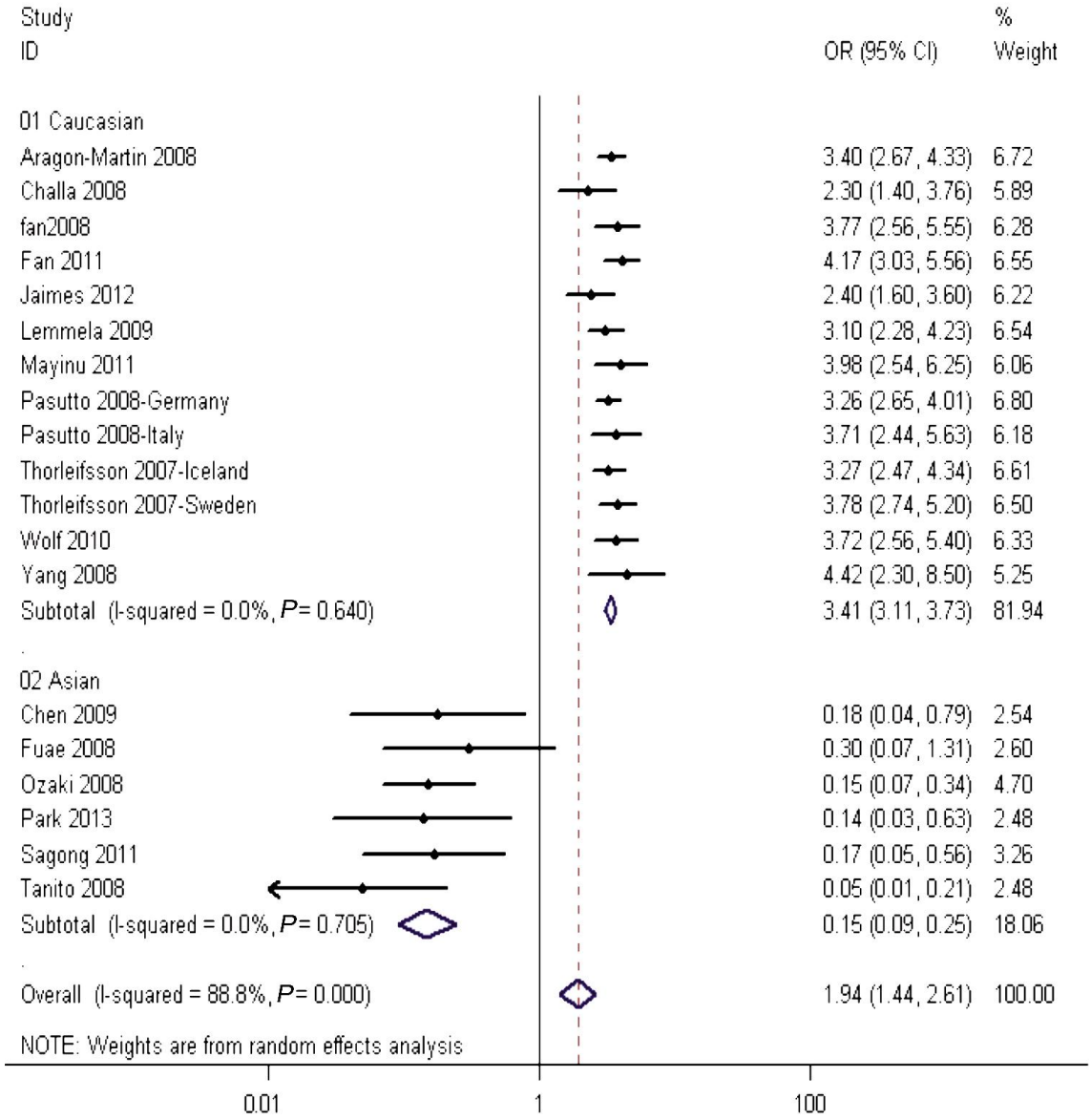

Figure 4 Forest plot from the Meta-analysis of single nucleotide polymorphism (SNP) rs2165241 and risk of XFS/XFG in allelic risk model (T *vs* C) for different ethnicities.

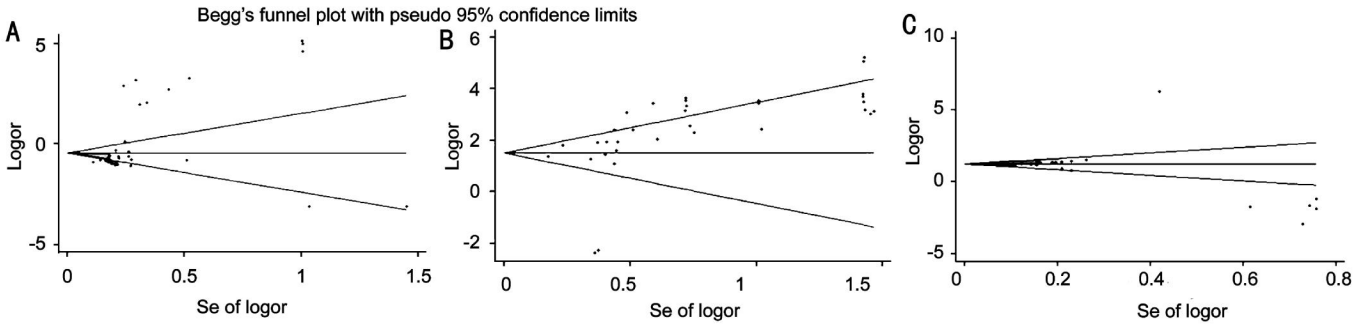

Figure 5 Begg's funnel plot for publication bias test, each circle represents a separate study for the indicated association. A: For rs1048661 polymorphism; B: For rs3825942 polymorphism; C: For rs2165241 polymorphism.

rs2165241) are associated with an increased risk for XFS/XFG in Caucasians, while rs1048661, rs2165241, but not rs3825942 polymorphisms have a potential protective effect on XFS/XFG in Asians. Furthermore, interaction between LOXL1 genes and other risk factors, such as age, sex, environmental factors, should also be considered in future studies, which should lead to a better understanding of the association between the LOXL1 polymorphisms and XFS/XFG risk.

ACKNOWLEDGEMENTS

Foundations: Supported by Natural Science Foundation of Guangdong Province (No.S2013010016037) and the National

Science and Tecnology Plan Project of China (973 program, No. 2011CB707501).
Conflicts of Interest: Ji QS, None; Qi B, None; Wen YC, None; Liu L, None; Guo XL, None; Yu GC, None; Zhong JX, None.

REFERENCES

1 Naumann GO, Schlotzer-Schrehardt U, Kuchle M. Pseudoexfoliation syndrome for the comprehensive ophthalmologist. Intraocular and systemic manifestations. *Ophthalmology* 1998;105(6):951-968

2 Ritch R. Exfoliation syndrome-the most common identifiable cause of open-angle glaucoma. *J Glaucoma* 1994;3(2):176-177

3 Ritch R, Schlötzer-Schrehardt U. Exfoliation syndrome. *Surv Ophthalmol* 2001;45(4):265-315

4 Schlötzer-Schrehardt U, Naumann GO. Ocular and systemic pseudoexfoliation syndrome. *Am J Ophthalmol* 2006;141(5):921-937

5 Sein J, Galor A, Sheth A, Kruh J, Pasquale LR, Karp CL. Exfoliation syndrome: New genetic and pathophysiologic insights. *Curr Opin Ophthalmol* 2013;24(2):167-174

6 Kenyon K, Modi WS, Contente S, Friedman RM. A novel human cdna with a predicted protein similar to lysyl oxidase maps to chromosome 15q24-q25. *J Biol Chem* 1993;268(25):18435-18437

7 Kim Y, Boyd CD, Csiszar K. A new gene with sequence and structural similarity to the gene encoding human lysyl oxidase. *J Biol Chem* 1995;270 (13):7176-7182

8 Thorleifsson G, Magnusson KP, Sulem P, Walters GB, Gudbjartsson DF, Stefansson H, Jonsson T, Jonasdottir A, Jonasdottir A, Stefansdottir G, Masson G, Hardarson GA, Petursson H, Arnarsson A, Motallebipour M, Wallerman O, Wadelius C, Gulcher JR, Thorsteinsdottir U, Kong A, Jonasson F, Stefansson K. Common sequence variants in the loxl1 gene confer susceptibility to exfoliation glaucoma. *Science (New York, NY)* 2007;317(5843):1397-1400

9 Lemmela S, Forsman E, Onkamo P, Nurmi H, Laivuori H, Kivel Puska P, Heger M, Eriksson A, Forsius H, Varilä I. Association of loxl1 gene with finnish exfoliation syndrome patients. *Ann Hum Genet* 2009;54(5): 289-297

10 Lee KY, Ho SL, Thalamuthu A, Venkatraman A, Venkataraman D, Pek DC, Aung T, Vithana EN. Association of loxl1 polymorphisms with pseudoexfoliation in the chinese. *Mol Vis* 2009;15:1120-1126

11 Chen L, Jia L, Wang N, Tang G, Zhang C, Fan S, Liu W, Meng H, Zeng W, Liu N, Wang H, Jia H. Evaluation of loxl1 polymorphisms in exfoliation syndrome in a chinese population. *Mol Vis* 2009;15:2349-2357

12 Tanito M, Minami M, Akahori M, Kaidzu S, Takai Y, Ohira A, Iwata T. LOXL1 variants in elderly Japanese patients with exfoliation syndrome/ glaucoma, primary open-angle glaucoma, normal tension glaucoma, and cataract. *Mol Vis* 2008;14:1898-1905

13 Ramprasad VL, George R, Soumittra N, Sharmila F, Vijaya L, Kumaramanickavel G. Association of non-synonymous single nucleotide polymorphisms in the LOXL1 gene with pseudoexfoliation syndrome in India. *Mol Vis* 2008;14:318-322

14 Chen H, Chen LJ, Zhang M, Gong W, Tam PO, Lam DS, Pang CP. Ethnicity-based subgroup meta-analysis of the association of LOXL1 polymorphisms with glaucoma. *Mol Vis* 2010;16:167-177

15 Boehringer S, Epplen JT, Krawczak M. Genetic association studies of bronchial asthma--a need for Bonferroni correction? *Hum Genet* 2000; 107(2):197

16 Pasutto F, Krumbiegel M, Mardin CY, Paoli D, Lämmer R, Weber BH, Kruse FE, Schlötzer-Schrehardt U, Reis A. Association of LOXL1 common sequence variants in German and Italian patients with pseudoexfoliation syndrome and pseudoexfoliation glaucoma. *Invest Ophthalmol Vis Sci* 2008;49(4):1459-1463

17 Ozaki M, Lee KY, Vithana EN, Yong VH, Thalamuthu A, Mizoguchi T, Venkatraman A, Aung T. Association of LOXL1 gene polymorphisms with pseudoexfoliation in the Japanese. *Invest Ophthalmol Vis Sci* 2008;49(9): 3976-3980

18 Mossbock G, Renner W, Faschinger C, Schmut O, Wedrich A, Weger M. Lysyl oxidase-like protein 1 (LOXL1) gene polymorphisms and exfoliation glaucoma in a central European population. *Mol Vis* 2008;14: 857-861

19 Mori K, Imai K, Matsuda A, Ikeda Y, Naruse S, Hitora-Takeshita H, Nakano M, Taniguchi T, Omi N, Tashiro K, Kinoshita S. LOXL1 genetic polymorphisms are associated with exfoliation glaucoma in the Japanese population. *Mol Vis* 2008;14:1037-1040

20 Mabuchi F, Sakurada Y, Kashiwagi K, Yamagata Z, Iijima H, Tsukahara S. Lysyl oxidase-like 1 gene polymorphisms in Japanese patients with primary open angle glaucoma and exfoliation syndrome. *Mol Vis* 2008;14: 1303-1308

21 Hewitt AW, Sharma S, Burdon KP, Wang JJ, Baird PN, Dimasi DP, Mackey DA, Mitchell P, Craig JE. Ancestral LOXL1 variants are associated with pseudoexfoliation in Caucasian Australians but with markedly lower penetrance than in Nordic people. *Hum Mol Genet* 2008;17(5):710-716

22 Hayashi H, Gotoh N, Ueda Y, Nakanishi H, Yoshimura N. Lysyl oxidase-like 1 polymorphisms and exfoliation syndrome in the Japanese population. *Am J Ophthalmol* 2008;145(3):582-585

23 Fuse N, Miyazawa A, Nakazawa T, Mengkegale M, Otomo T, Nishida K. Evaluation of LOXL1 polymorphisms in eyes with exfoliation glaucoma in Japanese. *Mol Vis* 2008;14:1338-1343

24 Fan BJ, Pasquale L, Grosskreutz CL, Rhee D, Chen T, DeAngelis MM, Kim I, del Bono E, Miller JW, Li T, Haines JL, Wiggs JL. DNA sequence variants in the LOXL1 gene are associated with pseudoexfoliation glaucoma in a U.S. Clinic-based population with broad ethnic diversity. *BMC Med Genet* 2008;9:5

25 Challa P, Schmidt S, Liu Y, Qin X, Vann RR, Gonzalez P, Allingham RR, Hauser MA. Analysis of LOXL1 polymorphisms in a United States population with pseudoexfoliation glaucoma. *Mol Vis* 2008;14:146-149

26 Aragon-Martin JA, Ritch R, Liebmann J, O'Brien C, Blaaow K, Mercieca F, Spiteri A, Cobb CJ, Damji KF, Tarkkanen A, Rezaie T, Child AH, Sarfarazi M. Evaluation of LOXL1 gene polymorphisms in exfoliation syndrome and exfoliation glaucoma. *Mol Vis* 2008;14:533-541

27 Fingert JH, Alward WL, Kwon YH, Wang K, Streb LM, Sheffield VC, Stone EM. LOXL1 mutations are associated with exfoliation syndrome in patients from the midwestern United States. *Am J Ophthalmol* 2007;144(6):

974-975

28 Wolf C, Gramer E, Muller-Myhsok B, Pasutto F, Gramer G, Wissinger B, Weisschuh N. Lysyl oxidase-like 1 gene polymorphisms in german patients with normal tension glaucoma, pigmentary glaucoma and exfoliation glaucoma. *J Glaucoma* 2010;19(2):136-141

29 Yang X, Zabriskie NA, Hau VS, Chen H, Tong Z, Gibbs D, Farhi P, Katz BJ, Luo L, Pearson E, Goldsmith J, Ma X, Kaminoh Y, Chen Y, Yu B, Zeng J, Zhang K, Yang Z. Genetic association of LOXL1 gene variants and exfoliation glaucoma in a utah cohort. *Cell cycle (Georgetown, Tex)* 2008;7 (4):521-524

30 Park do Y, Won HH, Cho HK, Kee C. Evaluation of lysyl oxidase-like 1 gene polymorphisms in pseudoexfoliation syndrome in a Korean population. *Mol Vis* 2013;19:448-453

31 Kasim B, Irkec M, Alikasifoglu M, Orhan M, Mocan MC, Aktas D. Association of LOXL1 gene polymorphisms with exfoliation syndrome/glaucoma and primary open angle glaucoma in a Turkish population. *Mol Vis* 2013;19:114-120

32 Micheal S, Khan MI, Akhtar F, Ali M, Ahmed A, den Hollander AI, Qamar R. Role of lysyl oxidase-like 1 gene polymorphisms in Pakistani patients with pseudoexfoliative glaucoma. *Mol Vis* 2012;18:1040-1044

33 Jaimes M, Rivera-Parra D, Miranda-Duarte A, Vasini B, Zenteno JC. Prevalence of high-risk alleles in the loxl1 gene and its association with pseudoexfoliation syndrome and exfoliation glaucoma in a Latin American population. *Ophthalmic Genet* 2012;33(1):12-17

34 Sagong M, Gu BY, Cha SC. Association of lysyl oxidase-like 1 gene polymorphisms with exfoliation syndrome in Koreans. *Mol Vis* 2011;17: 2808-2817

35 Rautenbach RM, Bardien S, Harvey J, Ziskind A. An investigation into LOXL1 variants in black south african individuals with exfoliation syndrome. *Arch Ophthalmol* 2011;129(2):206-210

36 Mayinu, Chen X. Evaluation of LOXL1 polymorphisms in exfoliation syndrome in the Uygur population. *Mol Vis* 2011;17:1734-1744

37 Malukiewicz G, Lesiewska-Junk H, Linkowska K, Mielnik M, Grzybowski T, Sulima N. Analysis of LOXL1 single nucleotide polymorphisms in Polish population with pseudoexfoliation syndrome. *Acta Ophthalmol* 2011;89(1):e64-66

38 Fan BJ, Pasquale LR, Rhee D, Li T, Haines JL, Wiggs JL. LOXL1 promoter haplotypes are associated with exfoliation syndrome in a U.S. Caucasian population. *Invest Ophthalmol Vis Sci* 2011;52(5):2372-2378

39 Williams SE, Whigham BT, Liu Y, Carmichael TR, Qin X, Schmidt S, Ramsay M, Hauser MA, Allingham RR. Major LOXL1 risk allele is reversed in exfoliation glaucoma in a black South African population. *Mol Vis* 2010;16:705-712

40 Abu-Amero KK, Osman EA, Dewedar AS, Schmidt S, Allingham RR, Al-Obeidan SA. Analysis of LOXL1 polymorphisms in a saudi arabian population with pseudoexfoliation glaucoma. *Mol Vis* 2010;16:2805-2810

41 Csiszar K. Lysyl oxidases: A novel multifunctional amine oxidase family. *Prog Nucleic Acid Res Mol Biol* 2001;70:1-32

42 Schlotzer-Schrehardt U, Hammer CM, Krysta AW, Hofmann-Rummelt C, Pasutto F, Sasaki T, Kruse FE, Zenkel M. LOXL1 deficiency in the lamina cribrosa as candidate susceptibility factor for a pseudoexfoliation-specific risk of glaucoma. *Ophthalmology* 2012;119(9):1832-1843