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Review Article

Association of glaucoma with risk of retinal vein occlusion: A meta-analysis

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ABSTRACT.

To summarize epidemiological evidences on the association between glaucoma and the risk of retinal vein occlusion (RVO). Relevant studies were identified by searching in PubMed, EMBASE and Cochrane until February 2018. Fifteen eligible observational studies were aggregated in this analysis. All results were analysed and pooled using random effects models with 95% confidence intervals (CI). In all studies, the odds ratio (OR) of glaucoma as a risk factor for RVO was 4.01 (95% CI: 3.28–4.91). In RVO subtype-differentiated subgroup analyses (six studies), the pooled OR showed that glaucoma was associated with central retinal vein occlusion (CRVO) (OR: 6.21; 95% CI: 4.64–8.31), branch retinal vein occlusion (BRVO) (OR: 2.38; 95% CI: 1.77–3.19) and hemiretinal vein occlusion (HRVO) (OR: 4.60; 95% CI: 2.26–9.35). In glaucoma-classified subgroup analyses (five studies), primary open-angle glaucoma (POAG) (OR: 5.03; 95% CI: 3.97–6.37) and chronic open-angle glaucoma (COAG) (OR: 2.36; 95% CI: 1.39–4.02) were significant risk factors for RVO development. There was a plausible relationship between primary angle closure glaucoma (PACG) and RVO risk (OR: 1.85; 95% CI: 0.41–8.35); to be precise, the OR was 5.3 in PACG and CRVO risk (95% CI: 1.04–26.95; p = 0.045), while the OR was 0.65 in PACG and BRVO risk (95% CI: 0.07–6.27; p = 0.707). To sum up, this meta-analysis shows that glaucoma is associated with the risk of RVO. Glaucoma should be kept in mind when investigating patients with RVO in the clinic.

Key words: glaucoma – meta-analysis – odds ratio – retinal vein occlusion

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Introduction

Retinal vein occlusion (RVO), a sight-threatening disorder, is recognized as the second morbidity in microvascular disease, such as retinopathy. It is generally classified as central retinal vein occlusion (CRVO) or branch retinal vein occlusion (BRVO) (Becker & Post 1951). In addition, when the superior or inferior half of the retina is involved in RVO, it is referred to as hemiretinal vein occlusion (HRVO) (Hayreh & Hayreh 1980). Retinal vein occlusion (RVO) is associated with older age, symptomatic ischaemic heart disease, higher systolic blood pressure and uncontrolled hypertension; however, the relationship between glaucoma and RVO is a topic of heated controversy. Traditionally, a close relationship between RVO and glaucoma has been emphasized. On the one hand, it is well known that RVO can increase the potential development of neovascular glaucoma (NVG) (Calugaru & Calugaru 2013). The development of NVG in CRVO, HRVO and BRVO is a serious and well-established complication, particularly in the CRVO (Beaumont & Kang 2002a; An & Kwon 2013). On the other hand, glaucoma is a known risk factor of RVO, as shown in many previous studies (Mitchell et al. 1996; Sperduto et al. 1998). An increased risk of BRVO and CRVO has been found in patients with a history of glaucoma. An intimate association has been affirmed between open-angle glaucoma (OAG) and RVO (EDCCS 1993; EDCCS 1996). However, more and more researchers have denied the accelerated effect of glaucoma in RVO risk. Some population-based studies have suggested that glaucoma is not related to RVO prevalence (Johnston et al. 1985; Klein et al. 2000; Jonas et al. 2013; Zhou et al. 2013).

Although numerous studies on this relationship have been published, uncertainties still exist about its course. Glaucoma is a worldwide epidemic that causes irreversible eye disease. The indistinct association between glaucoma and RVO confuses clinical judgments. Therefore, we conducted a systematic review for relevant studies that reported the relationship between glaucoma and RVO risk. The main purpose of this study was to investigate the effects of glaucoma on RVO incidence by meta-analysing the collected studies and to provide more reliable and more evidential data for clinical diagnosis.

Materials and Methods

Search strategy and selection criteria

We (XY and JL) conducted a literature search by searching the electronic databases PubMed, EMBASE and Cochrane until February 2018. The search strategy combined medical subject heading terms and the keywords "RVO" AND "glaucoma." Additionally, a manual detection of the possible studies was performed using the obtained articles' reference lists.

This systematic review included all the relevant observational studies which reported the association between glaucoma and RVO risk. The inclusion criteria of this study were as follows: (1) accorded with case-control, cohort, randomized control trial (RCT) or cross-sectional study design; (2) reported the association of glaucoma and RVO risk; and (3) presented an odds ratio (OR) with confidence interval (CI) or original data which could be used to determine OR values. We excluded studies in which only increasing intraocular pressure was reported.

Data extraction

We extracted the data independently from each eligible study. The following information was extracted from all included studies: the name of the first author, year of publication, study site and design, sample size (cases/controls or total), adjusting factor and the OR with 95% CI. All disagreements regarding data extraction were resolved through discussion.

Quality evaluation

There is no standard scale for evaluating the quality of various observational research in published studies. Therefore, we developed a new modified scoring system based on Newcastle–Ottawa Scale (NOS) (Cota et al. 2013; Zeng et al. 2015). The details were as follows: (1) defined the study design (case-control, cohort study or RCT, 1 point; cross-sectional study, 0 points), (2) met the inclusion list (yes, 1 point; no, 0 points), (3) stated the study period (yes, 1 point; no, 0 points), (4) included a diagnosis of RVO based on fundal examination or fundal photography (yes, 1 point; no, 0 points), (5) indicated follow-up duration for all subjects (yes, 1 point; no, 0 points), (6) provided general factors (age, gender, study site, etc.) (yes, 1 point; no, 0 points), (7) indicated adjustment status (yes, 1 point; no, 0 points) and (8) general influence characteristics were matched in the control group (yes, 1 point; no, 0 points). Studies that scored over 5 points provided higher methodological quality.

Statistical analysis

In our meta-analysis, we assessed the relationship between glaucoma and RVO risk by extracted ORs and the 95% CI from all the selected studies. The random effects model was used to estimate adjusted ORs, and the 95% CI was used to avoid the existing significant heterogeneity. Additionally, we used the I^2 method to detect heterogeneity. A p value less than 0.1 or I^2 greater than 50% was considered evidence of significant heterogeneity. Then, we conducted the subgroup analyses by RVO group (CRVO, BRVO and HRVO). Furthermore, more classified analyses were conducted by glaucoma classification (POAG, COAG and PACG), study design type (cohort studies, case-control studies, RCT and cross-sectional studies), study site and adjustment status.

A sensitivity analysis was performed to observe the influence of each study in the final pooled results. Both the funnel plot and Egger's test were used to detect potential publication bias. An asymmetric plot or p value <0.05 demonstrated the possible existence of publication bias. We used STATA software (version 12.0; Stata Corp, College Station, Texas) to perform all analyses. A p value <0.05 was considered to be statistically significant.

Results

A total of 2273 published articles (814 from PubMed, 1447 from EMBASE and 12 from Cochrane) were identified. First, 551 duplicates were excluded. After reviewing the titles and abstracts of 1722 articles, we excluded 1645 unrelated articles. The remaining 77 articles received a second screening, and 62 articles without outcomes of interest were excluded. Finally, 15 full-text articles were identified as eligible for the meta-analysis. Figure 1 demonstrates the steps of the literature search process.

The characteristics of all the included studies are shown in Table 1. Of the 15 included studies, nine were case-control studies, four were cohort studies, one was an RCT study and one was a cross-sectional study. Regarding study site distribution, 10 of the studies were from America, one was from Europe, one was from Australia and three were from Asia. The RVO subtype group was classified in six studies, and the glaucoma subtype group was classified in five studies. The range of research periods was 1977–2015, with

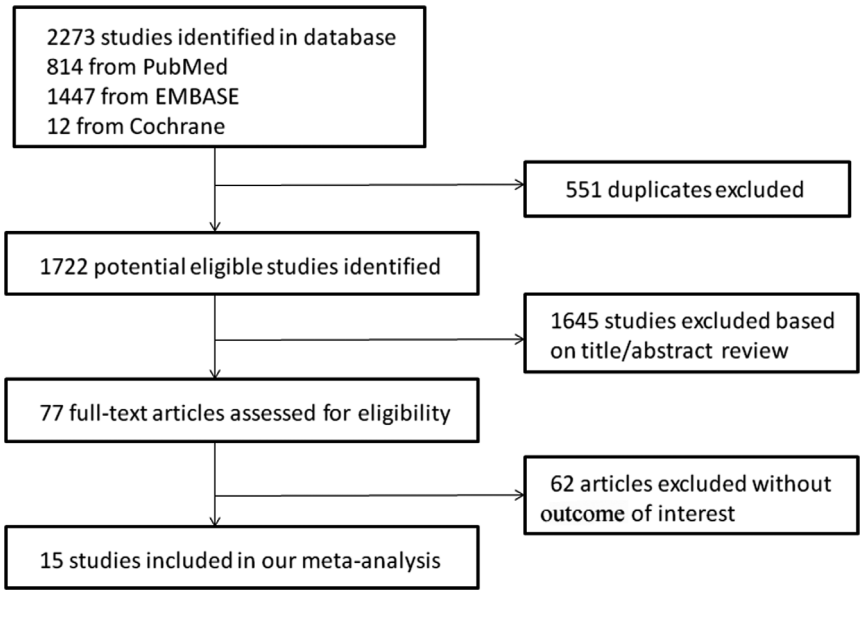

Fig. 1. Flow diagram of the literature search and selection process.

Table 1. Characteristics of eligible studies

Author (Year)	Study design	Study period	No.of case/control	Country	Adjustment/Match	Glaucoma group	Retinal vein occlusion group	OR (95%CI)
Johnston et al. (1985)	Case-control	1977–1982	225/100	USA	Age	COAG	BRVO	1.9 (0.9–4.13)
Rath et al. (1992)	Case-control	1985–1990	87/87	USA	Age, DM, family history	COAG	RVO	2.9 (1.38–6.05)
EDCCS (1993)	Case-control	1986–1990	270/1142	USA	Age, gender, race, clinic	Glaucoma	BRVO	2.5 (1.5–4.2)
EDCCS (1996)	Case-control	1986–1991	258/1142	USA	Age, gender, race, clinic	Glaucoma	CRVO	5.4 (3.5–8.5)
Mitchell et al. 1996;	Cohort	1992–1994	3654	Australia	Age	Glaucoma	RVO	4.3 (2.1–9.1)
Sperduto et al. (1998)	Case-control	1986–1990	607/1142	USA	Age, gender, race, clinic and other variable factors	Glaucoma	HRVO	4.6 (2.3–9.5)
						Glaucoma	CRVO	5.8 (3.7–9.1)
						Glaucoma	BRVO	2.5 (1.5–4.2)
Klein et al. (2000)	Cohort	198801995	4926	USA	Age	Glaucoma	RVO	2.43 (0.54–10.95)
Shahsuvaryan et al. (2003)	Case-control	1990–2001	408/566	Armenia	Sex, location, systemic diseases	Glaucoma	RVO	6.1 (3.8–9.1)
Koizumi H et al. (2007)	Case-control	2005–2006	144/144	USA	Hypertension, diabetes, angiotensin-converting, enzyme inhibitor use, and oestrogen use	Glaucoma	RVO	4.75 (2.33–9.71)
Klein et al. (2008)	Cohort	1987–1995	2119	USA	Age, retinal focal arteriolar narrowing, serum creatinine level 1.4 mg/dL, history of barbiturate use, serum phosphorus level, serum ionized calcium level	Glaucoma	RVO	3.17 (1.5–6.69)
Thapa R et al. (2010)	Case-control	2007–2008	248/300	Nepal	Age, sex, geographically	Glaucoma	RVO	3.7 (1.42–9.61)
						POAG	RVO	5.77 (1.61–20.69)
						PACG	RVO	1.85 (0.41–8.35)
						POAG	BRVO	3.3 (0.78–14.09)
						PACG	BRVO	0.65 (0.07–6.27)
						POAG	CRVO	13.33 (3.34–53.20)
						PACG	CRVO	5.3 (1.04–26.95)
Barnett et al. (2010)	Rct	2002–2005	1636	USA	Follow-up time	POAG	RVO	4.4 (1.7–11.34)
Shin et al. (2016)	Cross-sectional	2008–2012	37982	Korea	Age, household income, education level, HbA1c, diabetes, pulse pressure, BMI, fasting glucose, hypertension, hypercholesterolaemia, history of stroke, CKD, history of cataract operation, and refractive errors	Glaucoma	RVO	1.6 (0.74–3.46)

Table 1. (Continued)

Author (Year)	Study design	Study period	No.of case/control	Country	Adjustment/Match	Glaucoma group	Retinal vein occlusion group	OR (95%CI)
Park et al. (2017)	Cohort	2002–2013	102534	Korea	Age, gender, income, residential area, hypertension, diabetes, mellitus, dyslipidaemia	POAG	RVO	5.05 (3.94–6.47)
Schwaber et al. (2018)	Case-control	2012–2015	214/856	USA	Age	Glaucoma	RVO	6.91 (4.08–11.7)

BRVO = branch retinal vein occlusion; CI = confidence interval; COAG = chronic open-angle glaucoma; CRVO = central retinal vein occlusion; EDCCS = the eye disease case-control study; HRVO = hemiretinal retinal vein occlusion; I^2 = index for heterogeneity of studies; OR = odds ratios; PACG = primary angle closure glaucoma; POAG = primary open-angle glaucoma; RVO = retinal vein occlusion.

the shortest study lasting only 1 year and the longest study lasting 11 years. The OR and 95% CI values were provided in each article. The details of adjusted/marched factors are shown in Table 1. A total of 160 791 individuals were enrolled in the current meta-analysis.

We evaluated the methodological quality of all included articles. The assessment scale, which is a new eight-point scale system that we created, is presented in the Quality Evaluation section. A relatively high quality (more than five points) was detected in all 15 pooled articles.

Figure 2–4 shows the association between glaucoma and risk for RVO. Using a random effect meta-analysis model, glaucoma was determined to be a risk factor for RVO (OR: 4.01; 95% CI: 3.28–4.91; $I^2 = 45.6\%$). A significant heterogeneity was detected when all the studies were included ($I^2 = 45.6\%$; p = 0.028). In advanced RVO subgroup studies (Figure 3), glaucoma was correlated with CRVO (OR: 6.21; 95% CI: 4.64–8.31; $I^2 = 0\%$), BRVO (OR: 2.38; 95% CI: 1.77–3.19; $I^2 = 0\%$) and HRVO (OR: 4.60; 95% CI: 2.26–9.35). There was a closer association found between glaucoma and CRVO than between glaucoma and BRVO. Additionally, in both the POAG (OR: 5.03; 95% CI: 3.97–6.37; p < 0.001; $I^2 = 0\%$) and COAG (OR: 2.36; 95% CI: 1.39–4.02; p < 0.001; $I^2 = 0\%$) groups, a significant relation was found between OAG and RVO risk. In contrast, no significant relationship was observed between PACG and the incidence rate of RVO (OR: 1.85; 95% CI: 0.41–8.35; p = 0.424).

When study design type analyses were conducted, a significant association was detected in all nine case-control studies (OR: 4.16; 95% CI: 3.20–5.41; p < 0.001; $I^2 = 51.9\%$), all four cohort studies (OR: 4.7; 95% CI: 3.77–5.87; p < 0.001; $I^2 = 0\%$) and the only one RCT study (OR: 4.4; 95% CI: 1.70–11.36; p = 0.002); however, an inverse association was found in the only cross-sectional study (OR: 1.60; 95% CI: 0.74–3.46; p = 0.232). Significant associations were demonstrated in all ten studies from America (OR: 3.86; 95% CI: 3.01–4.94; p < 0.001; $I^2 = 38.2\%$), all three studies from Asia (OR: 3.28; 95% CI: 1.57–6.87; p = 0.002; $I^2 = 74.7\%$), the only one study from Europe (OR: 6.10; 95% CI: 3.94–9.44; p < 0.001) and the only one study from Australia (OR: 4.3; 95% CI: 2.01–8.95; p < 0.001) between glaucoma and RVO risk. Furthermore, a significant relationship between glaucoma and RVO incidence was observed in age adjusted, age unadjusted, gender adjusted and gender unadjusted groups, respectively (Table 2).

Only two studies supplied the OR between glaucoma classifications and RVO subtypes. In the POAG and COAG subgroups, the OR was 13.30 for the CRVO group (95% CI: 3.34–53.20; p < 0.001) and 2.14 for the BRVO group (95% CI: 1.09–4.20; p = 0.027). In the PACG subgroup, the OR was 5.3 for the CRVO group (95% CI: 1.04–26.95; p = 0.045) and 0.65 for the BRVO group (95% CI: 0.07–6.27; p = 0.707). Different associations were observed between glaucoma subtypes and RVO subtypes.

For the sensitivity analysis, we found no significant changes in the outcome when any article was excluded from the current meta-analysis. Furthermore, no significant publication bias was detected in the 15 studies using Begg's funnel plot (symmetrical), Begg's test (p = 0.075) or Egger's test (p = 0.068) (Figure 4).

Discussion

Retinal vein occlusion (RVO) is one of the most common retinal vascular disorders. In previous studies, the prevalence of RVO has been as high as 4.6% in adults 80 years or older (Cugati et al. 2006). Determining the risk factors of RVO will benefit clinical diagnosis and prognosis. Many studies have analysed the relationship between glaucoma and RVO risk. However, there have been contradictory outcomes in the research regarding the association between glaucoma and the risk for RVO. In the Blue Mountains Eye Study (BMES), glaucoma was defined as a core risk factor for RVO (Cugati et al. 2006). In contrast, when controlling for age, the incidence of RVO was not associated with glaucoma in the Beaver Dam Eye Study (Klein et al. 2000) or Singapore Malay Eye Study (Lim et al. 2008). The indistinct association between glaucoma and RVO can confuse clinical judgments. Therefore, we conducted a systematic review for relevant studies to analyse the relationship between glaucoma and RVO risk.

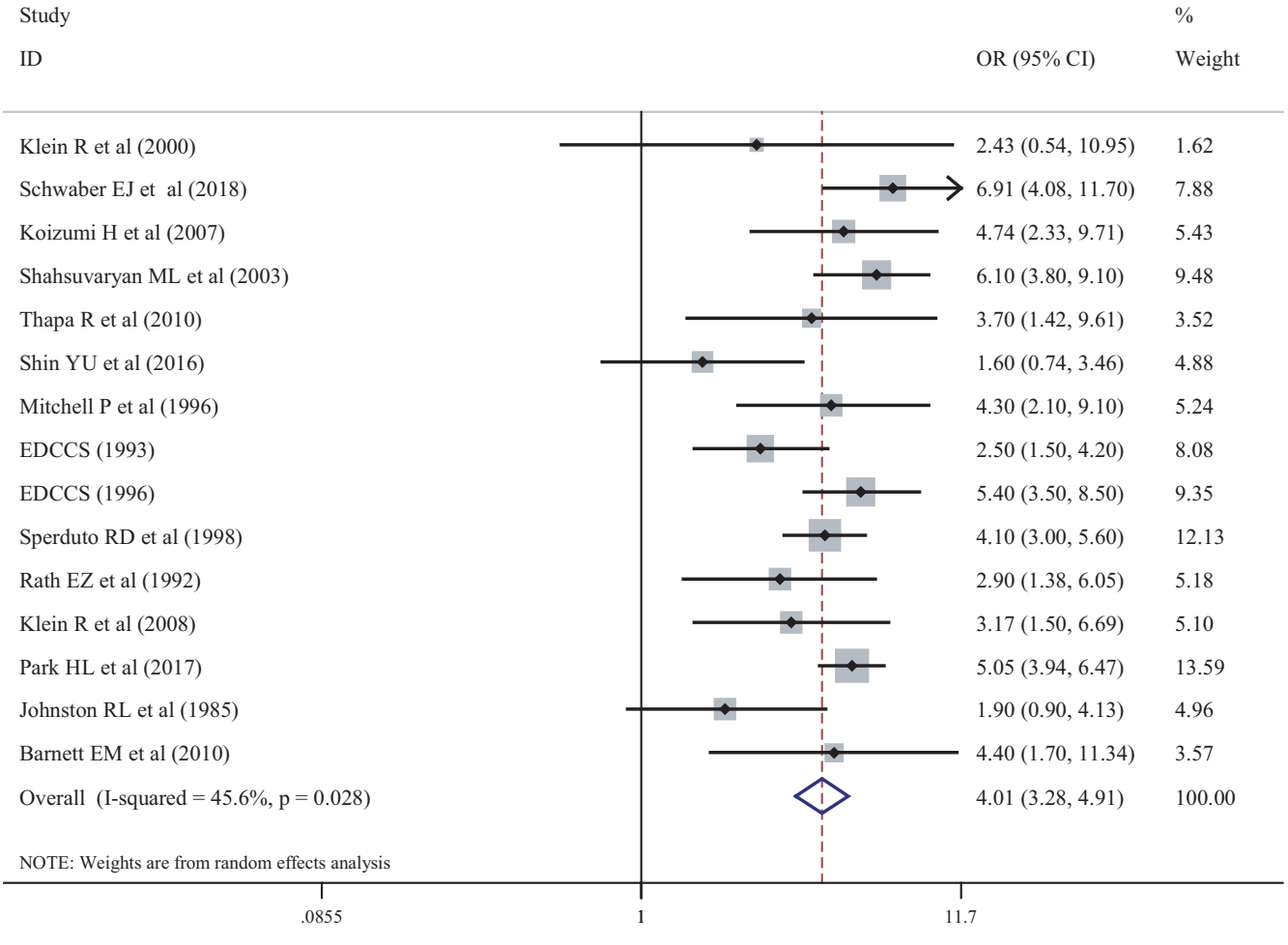

Fig. 2. Summary of the odds ratios (OR) for the association between glaucoma and the risk of retinal vein occlusion. CI = confidence interval. I^2 = index for heterogeneity of studies.

In the random effect model, glaucoma was found to be a risk factor for RVO (OR: 4.01; 95% CI: 3.28–4.91; I^2 = 45.6%) in 15 studies with high methodological quality. A few different potential hypotheses might explain this phenomenon. Primarily, Kim et al. (2011) suggested that the pathogenesis of RVO is likely associated with glaucomatous anatomic changes. In addition, Sonnsjo & Krakau (1993) presented a vascular hypothesis of glaucoma. Glaucoma individuals, including those with PACG and POAG, have narrower retinal arteries and veins than normal subjects (Gao et al. 2015). Therefore, retinal vein occlusion occurs secondarily to glaucomatous structural changes or coexists with retinal hemodynamic abnormality (Rubinstein & Jones 1976). In advanced subgroup analyses, glaucoma was proven to be associated with RVO to varying degrees depending on classification (CRVO, BRVO and HRVO). A higher rate of glaucoma was found in patients with optic cup RVO (abrupt dilatation changes in the calibre of the obstructed vein occurring at the optic cup) and optic nerve RVO (the occluded vein enters the lamina cribrosa as a dilated vein) without optical nerve head swelling than in patients with arteriovenous crossing RVO (Beaumont & Kang 2002b). This clinical phenomenon is suitable to explain why CRVO is more common in the glaucoma population. This is the first meta-analysis on the relationship between glaucoma and risk factors for RVO, and the harmful effect of glaucoma in RVO development was verified.

In another subgroup analysis by glaucoma classification, POAG and COAG were associated with RVO risk. It has been hypothesized that elevated intraocular pressure may compress vessel walls and cause subsequent blood vein intimal proliferation, leading to collapse of retinal capillaries (Luntz & Schenker 1980; Frucht et al. 1984). Furthermore, scientists have already declared that OAG precedes vascular occlusion (Bertelsen 1961; Barnett et al. 2010; Thapa et al. 2010; Park et al. 2017). In fact, disc haemorrhage is frequently seen in patients with OAG in the clinic. It is acknowledged that disc haemorrhage represents small vein occlusions. For this reason, researchers have hypothesized that OAG, retinal vein occlusion and disc haemorrhage might share a common pathogenesis (Hayreh 1994). Therefore, the vascular aetiology of OAG facilitates the development of RVO. However, the relationship between PACG and retinal vein occlusion needs to be evaluated further. On the one hand, retinal vessel parameters are quite different for PACG and POAG.

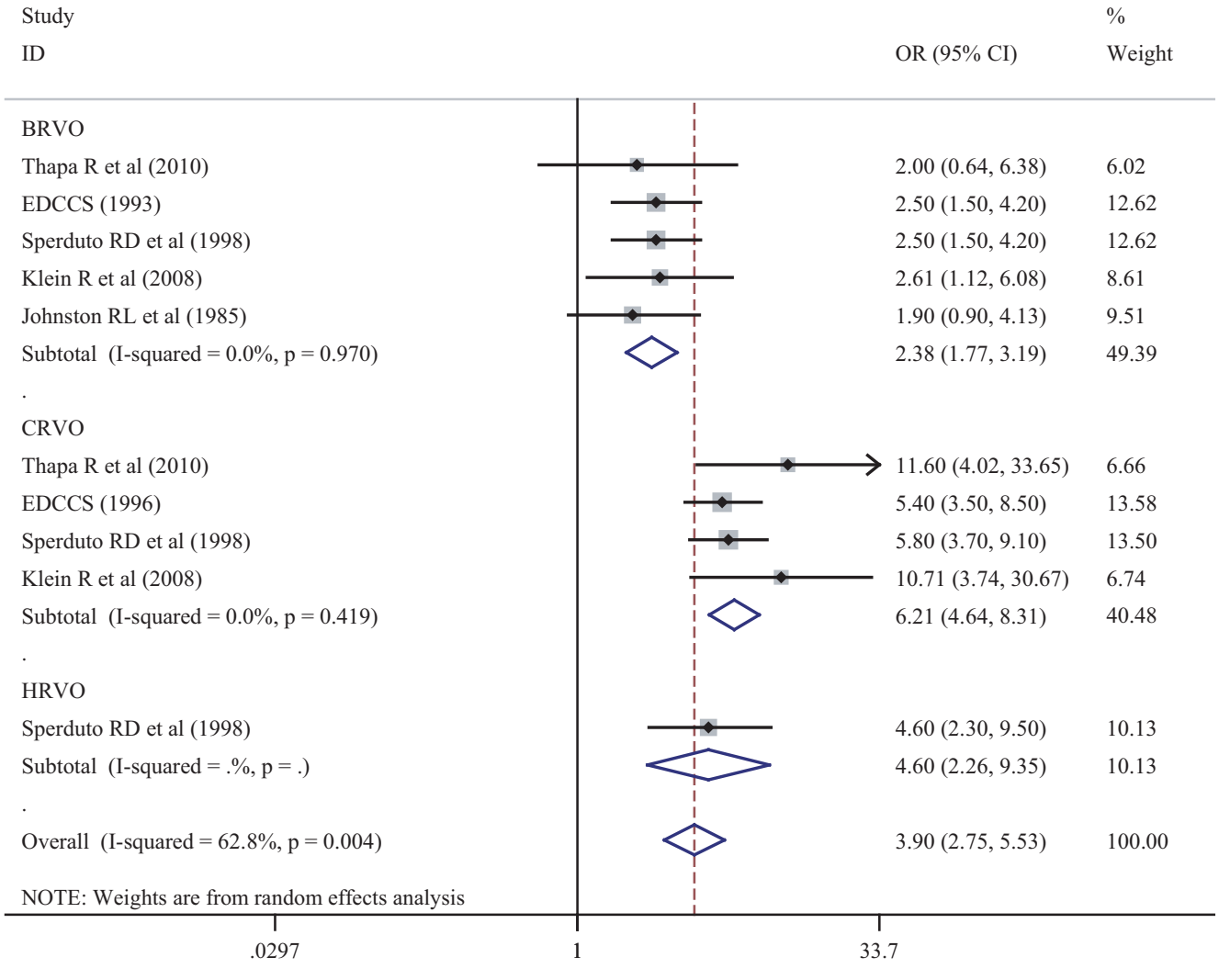

Fig. 3. Summary of the odds ratios (OR) for the association between glaucoma and the risk of retinal vein occlusion by subgroup analysis. CI: confidence interval. I^2: index for heterogeneity of studies.

Retinal vessel oxygenation and vessel calibre in PACG are relatively higher than POAG and NTG (Cheng et al. 2016). A vascular glaucoma model is more appropriate for the pathogenesis and disease process of POAG than PACG. On the other hand, the pathogenesis of PACG and POAG is fundamentally different. A shallow anterior chamber and narrow anterior chamber angle are unique to PACG, unlike POAG. The abnormality in the anterior chamber of PACG may be the main factor causing RVO. A narrow anterior chamber angle and shallower anterior chamber depth have been defined as important ocular factors associated with RVO (Jonas et al. 2013; Mohammadi et al. 2015). The overall small number of articles regarding RVO in PACG limits the power to detect meaningful associations for PACG and RVO risk. More large-scale prospective studies with PACG and RVO incidence are still warranted to clarify the association.

Of all 15 studies, six differentiated the RVO subtype (CRVO, HRVO and BRVO), and five classified the glaucoma subtype (PACG and POAG/COAG). In these studies, glaucoma was linked to the development of CRVO, whereas this association appears to be less clear for BRVO. Furthermore, only two studies illustrated the relationship between RVO subtypes and glaucoma subtypes thus far. In these two studies, OAG (POAG/COAG) was found to be a significant risk factor for CRVO (OR: 13.33; 95% CI: 3.34–53.20; $p < 0.001$) and BRVO (OR: 2.14; 95% CI: 1.09–4.20; $p = 0.027$). We assumed that OAG might be an obvious risk factor for CRVO and BRVO, especially for the former. However, PACG was associated with CRVO (OR: 5.3; 95% CI: 1.04–26.95; $p = 0.045$) but might not be a significant risk factor for BRVO (OR: 0.65; 95% CI: 0.07–6.27; $p = 0.707$). The weakest correlation was found between PACG and BRVO. Hayreh (2005) and Hayreh et al. (2004) also assumed that primary angle closure (PAC)/PACG induces RVO through a mechanism similar to that of POAG. In a retrospective study, angle closure was hypothesized to be associated with retinal vein occlusions, especially CRVO/HRVO (Michaelides & Foster 2010). In previous studies, the prevalence of PACG was 1.72% in BRVO and 5.3% in CRVO (Posner 1958; Vannas & Tarkkanen 1960; Vannas 1961); however, no significant difference was found between the two

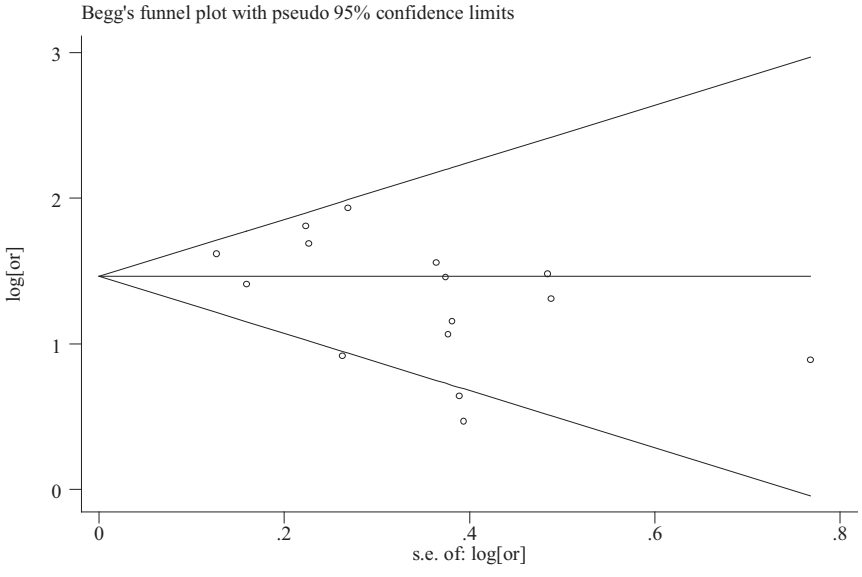

Fig. 4. Funnel plot for the association between glaucoma and the risk of retinal vein occlusion in all the included studies. p for bias = 0.075 in Begg's test and p for bias = 0.068 in Egger's test. Diamond: the pooled estimate of the ORs.

groups due to the small number of subjects included in these studies. Researchers also reported a higher frequency of PAC/PACG in RVO than in the general population, but the frequency of PAC/PACG in BRVO (3.1%) was similar to that of the general population (3.9%) (He et al. 2006; Wang et al. 2010). Due to the small number of studies enrolled in this subgroup analysis, more data from high-quality epidemiologic studies are needed in the future to confirm the reliability of these results. In all the published research, there was a plausible relationship between PACG and BRVO risk. Nonetheless, it is clear that PACG is more closely related to CRVO risk than to BRVO risk.

The results of the subgroup analysis, pooling case-control, cohort and RCT studies indicate that glaucoma is certainly associated with the risk for RVO. But there was one cross-sectional study confirming the non-association between glaucoma and RVO: the Korean National Health and Nutritional Examination Survey (Shin et al. 2016). However, considering that this cross-sectional study design presented a weaker power to detect correlations, this observation should be assessed by more reliable studies. Meanwhile, the additional analyses by adjustment status and study site did not provide results to the contrary. The only deficiency in our current meta-analysis is that certain inevitable limitations existed. On the one hand, in all observational studies pooled in this study, one of them consisted of cross-sectional design. The cross-sectional design is considered to demonstrate a weaker power to detect correlations. On the other hand, heterogeneity was unavoidable. In this study, the research periods ranged from 1977 to 2015. Even so, we suggest that research period did not have an impact on the quality of the data of the current analysis. Firstly, there have been no dramatic changes in the diagnostic standards of RVO or glaucoma in recent decades. Secondly, all of the studies in this meta-analysis met the inclusion criteria, and no single study had an obvious effect on the conclusion.

In summary, the meta-analysis demonstrated that glaucoma is a

Table 2. Subgroup analysis of glaucoma and risk of retinal vein occlusion

			Summary Effect		Study Heterogeneity	
Factors	Subgroups	No. of studies	OR (95% CI)	p Value	I^2, %	P Value
RVO subtype	BRVO	5	2.38 (1.77–3.19)	<0.001	0	0.97
	CRVO	4	6.21 (4.64–8.31)	<0.001	0	0.419
	HRVO	1	4.60 (2.26–9.35)	<0.001	-	-
Glaucoma subtype	POAG	3	5.03 (3.97–6.37)	<0.001	0	0.675
	COAG	2	2.36 (1.39–4.02)	<0.001	0	0.435
	PACG	1	1.85 (0.41–8.35)	0.424	-	-
Study type	RCT	1	4.40 (1.70–11.36)	0.002	-	-
	Case-control	9	4.16 (3.20–5.41)	<0.001	51.9	0.034
	Cross-sectional	1	1.60 (0.74–3.46)	0.232	-	-
	Cohort	4	4.70 (3.77–5.87)	<0.001	0	0.535
Study site	Europe	1	6.10 (3.94–9.44)	<0.001	-	-
	Asia	3	3.28 (1.57–6.87)	0.002	74.7	0.019
	America	10	3.86 (3.01–4.94)	<0.001	38.2	0.104
	Australia	1	4.3 (2.01–8.95)	<0.001	-	-
Adjustment status	Age adjusted	12	3.73 (2.94–4.72)	<0.001	52.1	0.018
	Age unadjusted	3	5.50 (3.89–7.78)	<0.001	0	0.74
Adjustment status	Gender adjusted	4	4.27 (3.25–5.60)	<0.001	56	0.078
	Gender unadjusted	11	3.76 (2.78–5.10)	<0.001	46.2	0.046

BRVO = branch retinal vein occlusion; CI = confidence interval; CRVO = central retinal vein occlusion; HRVO = hemiretinal retinal vein occlusion; I^2 = index for heterogeneity of studies; OR = odds ratio; RVO = retinal vein occlusion.

significant risk factor for RVO. It was indicated that OAG (POAG/COAG) could increase the incidence of RVO, particularly for CRVO. Meanwhile, there was less association between PACG and RVO, especially for BRVO. The outcome of our meta-analysis is meaningful for clinical judgments. The controversial results should be clarified with large-scale prospective and high-quality epidemiologic studies in the future.

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