Systematic Review

Prevalence of Depression and Anxiety Disorders in Patients with Glaucoma: A Systematic Review and Meta-Analysis Based on Cross-Sectional Surveys

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Abstract

Objective: Glaucoma is a chronic disease with an insidious onset that often brings severe psychological burden to patients. Therefore, based on a systematic review and meta-analysis, we explore the prevalence and severity of depression and anxiety in glaucoma patients, and provide clinically valuable information for medical staff.

Methods: Computer searches were conducted for relevant studies in PubMed, Embase, ProQuest PsycINFO, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Web of Science, The Cochrane Library, Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure, Wanfang Database, and China VIP Database. The search date range was from the establishment of the database to December 2023. Literature was screened and data were extracted. The Cochrane risk of bias assessment tool was used to evaluate the quality of the literature, and RevMan5.4 was used for meta-analysis.

Results: The total sample size of the 15 included studies was 24,334 cases. All included studies were of high quality. The results of the meta-analysis revealed that, compared with control patients without glaucoma, patients with glaucoma were more likely to experience depression and to have more severe depressive symptoms [RR (Relative Risk) = 5.92, 95% CI (Confidence Interva) (3.29, 10.66), $p < 0.01$]; they were also more likely to experience anxiety and to have more severe anxiety symptoms [RR = 2.99, 95% CI (1.93, 4.64), $p < 0.01$]. The results of the sensitivity analysis showed that the two studies by Cumurcu E. 2005 and Yochim 2012 were the sources of heterogeneity in the meta-analysis of depression; and the three studies by Mabuchi 2012, Otori 2017, and Yochim 2012 were the sources of heterogeneity in the meta-analysis of anxiety disorders.

Conclusion: People with glaucoma are more likely to experience depression and anxiety than people without glaucoma. Medical staff should pay greater attention to patients' emotional problems and help patients improve their quality of life.

Keywords

glaucoma; depression; anxiety; meta-analysis; bad mood; mental health

Introduction

Glaucoma is the name given to a group of slowly progressive eye diseases associated with characteristic damage to the optic nerve at the back of the eye. Glaucomatous optic neuropathy is accompanied by typical visual field damage; if not treated in time, it will lead to optic nerve atrophy, optic papilla depression and accompanying visual field defects, vision loss, and eventually blindness [1]. According to the state of the anterior chamber angle (closed or open) when intraocular pressure rises, primary glaucoma is divided into two types: primary angle-closure glaucoma and

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primary open-angle glaucoma. Glaucoma disease affects patients' quality of life in multiple ways; it impairs visual function (reduced peripheral vision and visual acuity), requires the use of intraocular pressure-lowering eye drops, brings inconvenience to patients' lives, causes adverse reactions to treatment, and increases patients' financial burden.

Glaucoma is a chronic disease with an insidious onset that often leads to severe visual impairment and even blindness. Therefore, glaucoma often brings a serious psychological burden to patients [2,3]. Anxiety and depression are two of the most common mood disorders experienced by people with glaucoma, and are often accompanied by physical symptoms. Previous studies have found that the prevalence of anxiety and depression in people with glaucoma is significantly higher than that in the normal population [4,5]. It has been reported in the literature that in Turkey [6] and Japan [7], the prevalence of anxiety among people with glaucoma is about 13.5%. However, the prevalence of depression among people with glaucoma varies greatly by region. In the United States [2] and Japan [7], it is about 10%, in Australia, it is about 19.09% [8], and in Turkey, it is as high as 24.66% [9] to 57% [6]. Therefore, it is critical to understand the connection between psychosocial factors and the onset of glaucoma.

Currently, few reports systematically evaluate the prevalence of depression and anxiety in patients with glaucoma. Therefore, we conducted a systematic review and meta-analysis, based on cross-sectional surveys, to evaluate the incidence and severity of depression and anxiety in patients with glaucoma. A better understanding of these relationships may provide valuable clinical information for medical staff that can be used to improve patients' physical and mental health, promote disease recovery, and improve their quality of life.

Methods and Materials

Literature Inclusion and Exclusion Criteria

Inclusion Criteria

This systematic review is reported according to PRISMA 2020 guidelines (**Supplementary File 1**). (a) Patients diagnosed with glaucoma that agreed to voluntarily participate in the study; (b) Classified as observational research; (c) Use of a standard evaluation scale as a tool to judge the results; (d) The age of the research subjects ≥18 years old.

Exclusion Criteria

(a) Studies where the full text is not available; (b) Studies where the research design is unreasonable, complete information is missing, or data cannot be obtained; (c) Studies are published repeatedly or have duplicate data; (d) The article is a review, case report, or pilot study; (e) The way of the results does not meet the standards; (f) Studies related to sleep and breathing disorders.

Outcome Assessment Tool

Scales used clinically to evaluate patients' depression include the Beck Depression Inventory (BDI) [10], Goldberg Anxiety and Depression Scale (GADS) [11], Geriatric Depression Scale (GDS) [12], Hospital Anxiety and Depression Scale (HADS) [13], Zung Self-Rating Depression Scale (SDS) [14], and Patient Health Questionnaire (PHQ) [15].

Scales used clinically to evaluate patients' anxiety include the Generalized Anxiety Disorder Questionnaire (GADQ) [16], Geriatric Anxiety Scale (GAS) [16], Goldberg Anxiety and Depression Scale (GADS) [11], State-Trait Anxiety Index (STAI) [17], Hospital Anxiety and Depression Scale (HADS) [13], and Zung Self-Rating Anxiety Scale (SAS) [18].

Literature Search Strategy

Computer searches were conducted on PubMed (https://pubmed.ncbi.nlm.nih.gov), Embase (https://www.embase.com), ProQuest PsycINFO (https://www.proquest.com/docview/1700283469?sourcetype=Trade%20Journals), CINAHL (https://www.ebsco.com/zh-cn/products/research-databases/cinahl-database), Web of Science (https://sci-hub.hkvisa.net/), The Cochrane Library (https://www.cochranelibrary.com/?contentLanguage=eng), Chinese Biomedical Literature Database (CBM) (http://www.sinomed.ac.cn/index.jsp), China National Knowledge Infrastructure (https://www.cnki.net/), Wanfang Database (https://www.wanfangdata.com.cn/index.html), and China VIP Database (https://www.cqvip.com/). The search date range is from the establishment of the database to December 2023. The search terms are: "glaucoma/anxiety disorder/depression/bad mood/depression rating scale/anxiety rating scale/psychological stress/social stress/low vision disease/mental health/psychological symptoms/mental health status". MeSH terms are: [Topic: (glaucoma) OR (anxiety disorder) OR (depression) OR (bad mood)] AND (Topic: mental state) AND [Topic:

Table 1. General data characteristics of the studies.

Author (year)	Nation	Case (n)	Control (n)	Outcomes assessed	NOS score	Scales used
Ayaki 2016 [20]	Japan	69	71	Depression, anxiety	9	HADS-D, HADS-A
Agorastos 2013 [21]	Germany	49	37	Depression, anxiety	9	BDI-II, STAI-T
Cumurcu E. 2005 [22]	Turkey	61	-	Depression, anxiety	7	HADS-D, HADS-A
Eramudugolla 2013 [23]	Australia	23	375	Depression, anxiety	9	GADS-D, GADS-A
Kong 2014 [24]	China	100	50	Depression, anxiety	8	SDS, SAS
Lim 2016 [25]	Singapore	100	-	Depression, anxiety	9	HAM-D, HAM-A
Ma 2015 [26]	China	120	120	Depression, anxiety	9	SDS, SAS
Mabuchi 2008 [7]	Japan	230	230	Depression, anxiety	7	HADS-D, HADS-A
Mabuchi 2012 [27]	Japan	408	-	Depression, anxiety	8	HADS-D, HADS-A
Otori 2017 [28]	Japan	472	-	Anxiety	8	STAI-S
Ra 2017 [29]	Japan	32	61	Depression, anxiety	9	HADS-D, HADS-A
Rezapour 2018 [30]	Germany	293	14,364	Depression, anxiety	9	PHQ-9, GAD-2
Thau 2018 [31]	United States	90	178	Depression	8	GDS-15
Wang S. 2012 [5]	United States	453	6,307	Depression	7	PHQ-9
Yochim 2012 [32]	United States	41	-	Depression, anxiety	9	GDS-15, GAI

NOTE: The total sample size was 24,334 cases and the control group was 21,793 cases.

NOS, Newcastle-Ottawa Scale; BDI, Beck Depression Inventory; GAD, Generalized Anxiety Disorder Scale; GAI, General Anxiety Inventory; GDS, Geriatric Depression Scale; GADS, Goldberg Anxiety and Depression Scale; HAM, Hamilton Anxiety and Depression Scale; HADS, Hospital Anxiety and Depression Scale; PHQ, Patient Health Questionnaire; STAI, State-Trait Anxiety Inventory; SAS, Zung Self-Rating Anxiety Scale; SDS, Zung Self-Rating Depression Scale.

(depression rating scale) OR (anxiety rating scale) OR (psychological stress) OR (social stress) OR (mental health)]. A joint search of subject words and free words was used, and a second expanded search was performed at the same time.

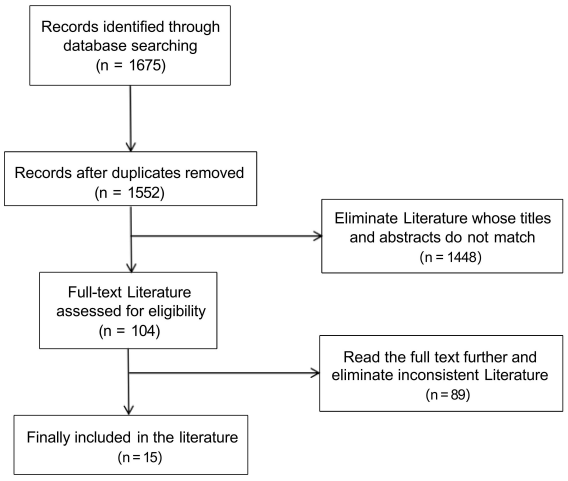

Fig. 1. Literature screening flow chart.

Literature Screening and Data Extraction

Two qualified researchers independently screened the literature, extracted data, and cross-checked it. If there were any differences, they were discussed and resolved, or the opinions of a third qualified researcher were sought. When screening literature, the title and abstract were read first, and after excluding irrelevant literature, the full text was read to determine whether to include it. The extracted content mainly included basic information about the included studies, baseline characteristics of the research subjects, intervention measures, and outcome indicators.

Literature Quality Assessment

Information extraction included the name of the first author, date of publication, study type, location, sample size, follow-up time, extent of lymph node dissection, and study endpoints. For non-randomized controlled studies, the Newcastle-Ottawa Scale (NOS) was used to assess quality; an NOS score $\geq$7 is considered a high-quality study [19].

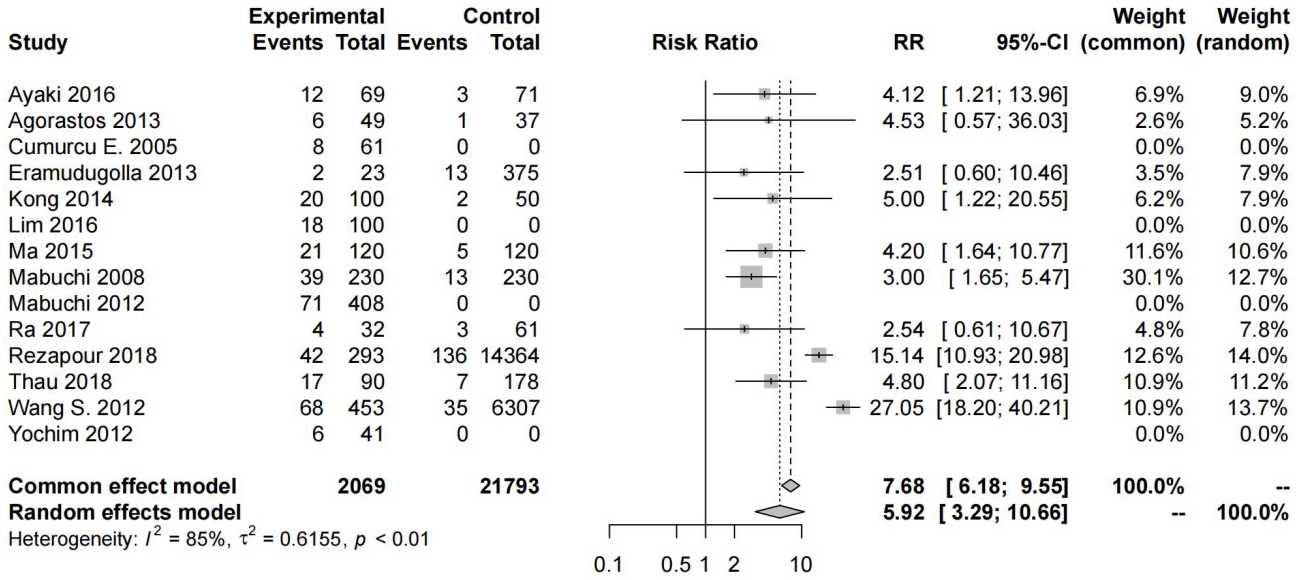

Fig. 2. Forest chart of the prevalence of depression in patients with glaucoma. RR, Relative Risk; CI, Confidence Interval.

Statistical Method

RevMan 5.4 software (the Cochrane Collaboration, London, Britain) was used for statistical analysis of the data. Measurement data are expressed as the weighted mean difference, the standardised mean difference (SMD), and their 95% confidence interval (CI). Heterogeneity among studies was evaluated using the Q test and I^2 value. If $p > 0.1$ and $I^2 < 50\%$, there was considered to be no statistical heterogeneity, and a fixed-effects model was used for meta-analysis. Otherwise, a random-effects model was used for meta-analysis, and subgroup analysis or one-by-one exclusion method was used for sensitivity analysis to further explore the source of heterogeneity. p values < 0.05 were considered statistically significant.

Results

Literature Search Results

The search yielded a total of 1675 studies in the database, and after excluding duplicate publications, there remained 1552 records. After screening the abstracts and titles, 104 studies related to the topic were obtained. After carefully reading the full text, 15 studies were finally included. The literature screening process is shown in Fig. 1.

Basic Characteristics of Included Literature

To better display the information included in the literature, we extracted their basic features one by one. The total sample size of the 15 included studies was 24,334 cases, involving 7 countries: 2 studies in Germany, 5 in Japan, 1 in Turkey, 1 in Australia, 2 in China, 1 in Singapore, and 3 in the United States. A total of 14 studies assessed patients for depression, and 13 studies assessed patients for anxiety disorders. All of the studies used standard scales as assessment tools for outcome indicators. Among all 15 included studies, 8 studies had a NOS score of 9 points, 4 studies had a NOS score of 8 points, and 3 studies had a NOS score of 7 points, indicating that the included studies were all high quality. The specific basic characteristics of all included studies are shown in Table 1 (Ref. [5,7,20–32]).

Prevalence of Depression in Patients with Glaucoma

We used meta-analysis to investigate the prevalence of depression in patients with glaucoma. The results of the meta-analysis showed large heterogeneity (I^2 = 85%), and a random-effects model was used for analysis. Compared with control patients without glaucoma, those with glaucoma were more likely to experience depression and had more severe depressive symptoms [Relative Risk (RR) = 5.92, 95% Confidence Interva (CI) (3.29, 10.66), $p < 0.01$] (Fig. 2). The difference between the two groups was statistically significant.

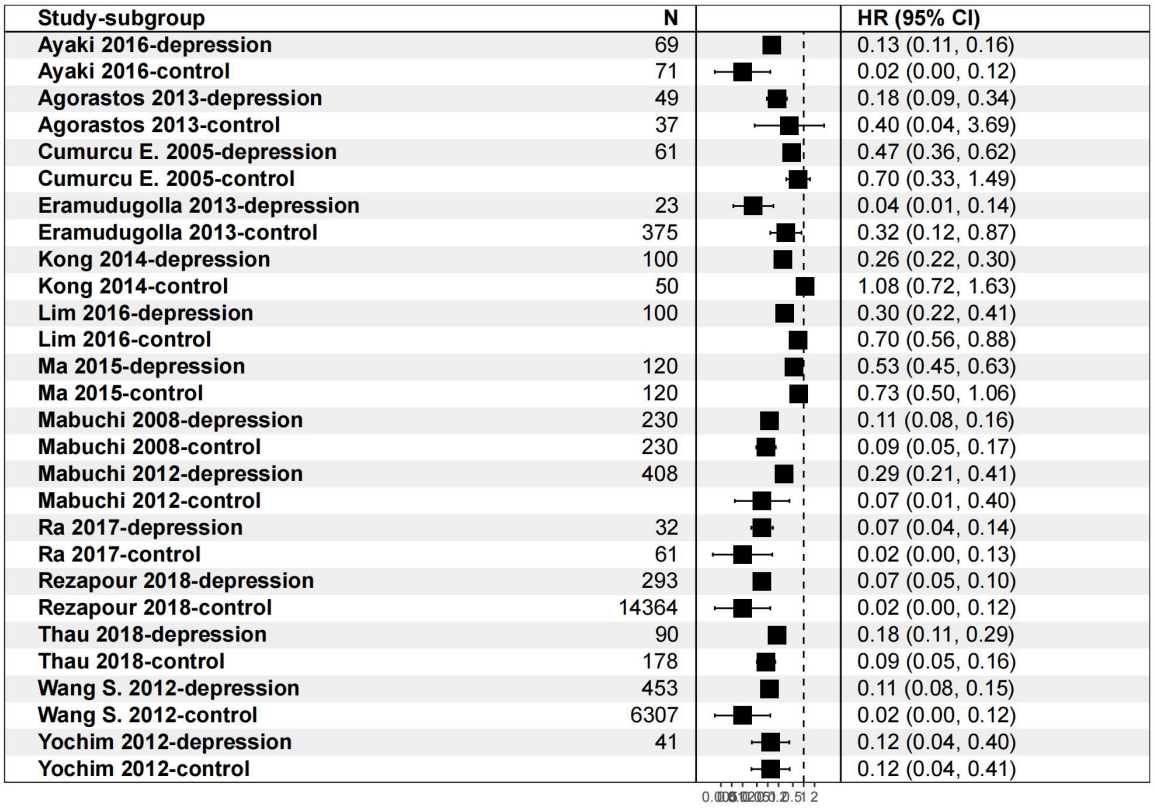

Fig. 3. Sensitivity analysis of depression in patients with glaucoma. HR, Hazard Ratio.

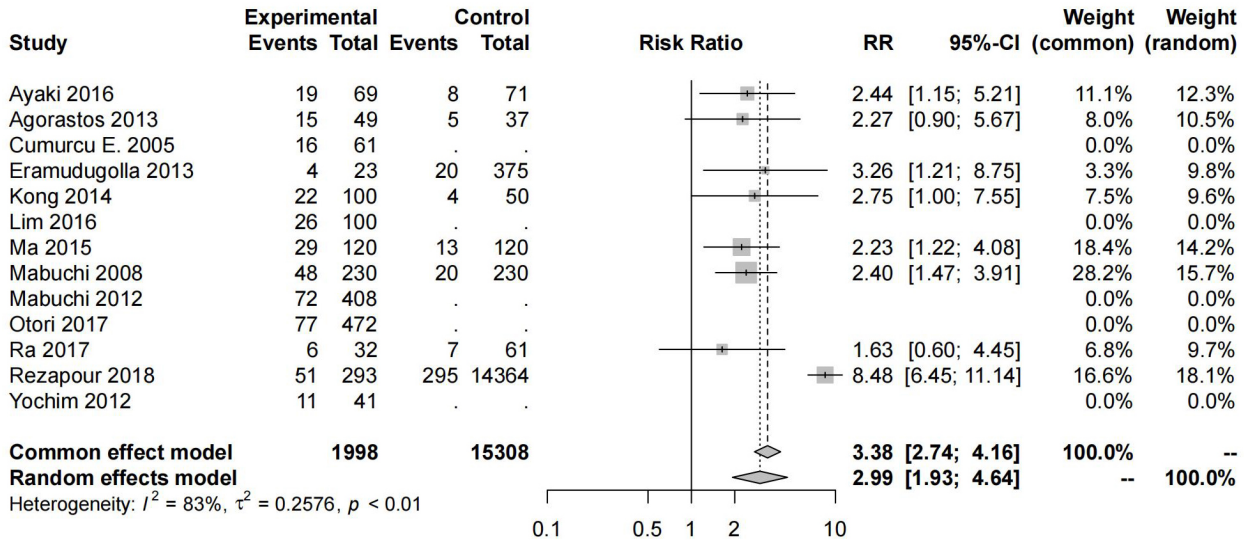

Fig. 4. Forest chart of the prevalence of anxiety in patients with glaucoma.

Sensitivity Analysis of Depression in Patients with Glaucoma

Since meta-analysis showed high heterogeneity, we used sensitivity analysis to identify the source of heterogeneity. The results of the sensitivity analysis of all 14 studies showed considerable heterogeneity ($I^2 = 78.8\%$, $p < 0.01$), indicating that certain studies were the source of heterogeneity in the meta-analysis (Fig. 3). We found that after excluding the studies of Cumurcu E. 2005 [22] and Yochim 2012 [32], the heterogeneity was 0%, indicating that these two studies were the source of heterogeneity.

Prevalence of Anxiety Disorders in Patients with Glaucoma

We used meta-analysis to explore the prevalence of anxiety in glaucoma patients. Meta-analysis results revealed high heterogeneity ($I^2 = 83\%$), and a random-effects model was used for analysis. Compared with control patients without glaucoma, patients with glaucoma were more likely to experience anxiety and had more severe anxiety symptoms [RR = 2.99, 95% CI (1.93, 4.64), $p < 0.01$] (Fig. 4). The difference between the two groups was statistically significant.

Sensitivity Analysis of Anxiety Disorders in Patients with Glaucoma

Sensitivity analysis was used to identify the sources of heterogeneity in the meta-analysis. The sensitivity analysis results of all 13 studies showed considerable heterogeneity ($I^2 = 95.6\%$, $p < 0.01$), indicating that certain studies were the source of heterogeneity in the meta-analysis (Fig. 5). It was found that after excluding the studies of Mabuchi 2012 [27], Otori 2017 [28], and Yochim 2012 [32], the heterogeneity was 0%, indicating that these three studies were the source of heterogeneity.

Discussion

Glaucoma is a group of common eye diseases that increase intraocular pressure and threaten the optic nerve and visual function. In China, the number of glaucoma patients is also relatively large, currently reaching 9.4 million. This is mainly because many people in China are over 50 years old. Recent research shows that glaucoma patients have poor psychological status [33]. In this study, the results of our meta-analysis showed that, compared to controls, 2541 glaucoma patients were more likely to experience depression [RR = 5.92, 95% CI (3.29, 10.66), $p < 0.01$] and anxiety [RR = 2.99, 95% CI (1.93, 4.64), $p < 0.01$], and that their symptoms were more severe. In addition, their depression and anxiety levels were positively correlated with the severity of glaucoma. However, because the association between glaucoma and depression or anxiety is complex, further research on the potential causal mechanisms is needed in the future. Furthermore, meta-studies should be conducted using larger sample sizes, and more reliable tools should be designed to assess psychological disorders. Ophthalmologists should also provide patients with accurate and appropriate information about glaucoma to prevent the development of excessive and inappropriate anxiety and depression.

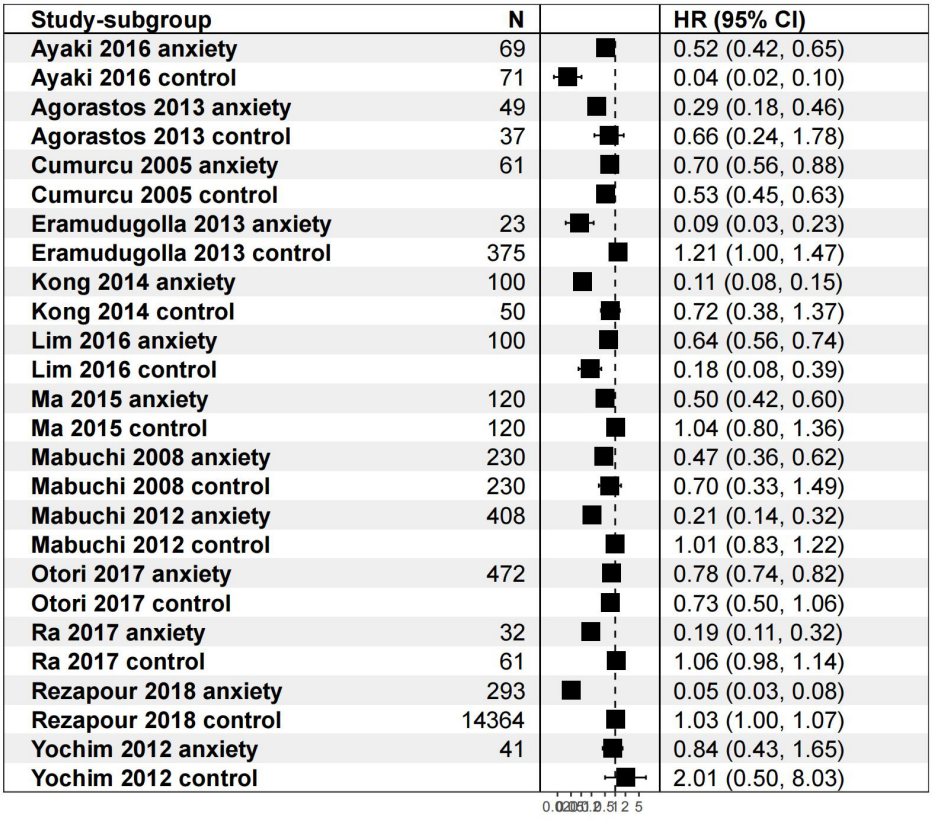

Fig. 5. Sensitivity analysis of anxiety disorders in patients with glaucoma.

Since the results of the meta-analysis showed great heterogeneity, we chose to use the random-effects model for analysis. However, after subgroup analysis and sensitivity analysis, we found that the heterogeneity was significantly reduced, which shows that the results of our meta-analysis are reliable. There are many potential sources of heterogeneity, such as different countries, regions, medical levels, different follow-up times, intervention times, different assessment scales, etc. Although all study outcome measures were measured using objective measurement methods, we believe that lack of blinding has little effect on bias in the results.

The limitations of this study are: (1) Some literature lacks systematic observation, so the final results may be biased; (2) The evaluation indicators selected in the study are all scale tools. We recommend that future studies include larger, higher-quality samples, with longer follow-up times, to improve the objectivity of the conclusions.

Conclusion

People with glaucoma are more likely to experience depression and anxiety than people without glaucoma. Future studies should attempt to infer the causal nature of this association, and to identify depression- and anxiety-related characteristics in these patients. To promote discussions about mental health among glaucoma patients, ophthalmologists, and optometrists should pay greater attention to patients' emotional issues, guide them to appropriate support services and help patients improve their quality of life.

Availability of Data and Materials

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Author Contributions

JFY: Conception, Design, Materials, Data Collection, Analysis, Literature Review, Writing. HJL: Design, Supervision, Materials, Data Collection, Analysis, Literature Review, Writing. NNG: Supervision, Materials, Data Collection, Analysis, Writing, Critical Review. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.62641/aep.v52i3.1561.

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