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Navigating the intersection of psychiatry and ophthalmology: A comprehensive review of depression and anxiety management in glaucoma patients

Mind and sight: A psychiatric-ophthalmologic perspective

Glaucoma, a prevalent and debilitating eye disease, has long been associated with vision impairment and blindness. However, recent research has shed light on the often-underestimated psychological dimensions of this condition. Anxiety and depression, two pervasive psychiatric comorbidities, have been increasingly recognized among glaucoma patients. This comprehensive review aims to explore the intricate relationship between psychiatry and ophthalmology, in the context of managing depression and anxiety in glaucoma patients. By meticulously examining peer-reviewed literature, we synthesize current knowledge on the prevalence, risk factors, and underlying mechanisms of anxiety and depression in glaucoma. The evidence reveals that glaucoma patients face an elevated risk of experiencing these mood disorders. Factors such as progressive vision loss, complex medication regimens, and the fear of further visual deterioration contribute to their vulnerability. Moreover, we delve into the bidirectional relationship between glaucoma and mood disorders, shedding light on the complex interplay between ocular and emotional health. Our review investigates the implications of anxiety and depression on glaucoma management, including their potential impact on treatment adherence, disease progression, and overall quality of life. We also explore the neurobiological pathways linking glaucoma and mood disorders, providing a foundation for future research and potential therapeutic interventions. In conclusion, recognizing the psychological burden carried by glaucoma patients is essential for holistic and patient-centered care. This review underscores the pressing need for integrated approaches that bring together ophthalmological and psychiatric expertise to optimize the well-being of individuals facing the challenges of glaucoma. By addressing anxiety and depression in glaucoma care, healthcare providers can enhance the overall quality of life for these patients, ultimately leading to

improved outcomes and a brighter future for those affected by this condition. This review offers valuable insight for healthcare practitioners and researchers, providing a concise overview of key topics and research in the field of managing depression and anxiety in glaucoma patients.

Key Words: Glaucoma; Psychiatry; Depression; Anxiety; Risk factors; Bidirectional relationship

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Core Tip: This literature review underscores the evolving perspective on glaucoma, traditionally viewed solely as an ocular ailment. It delves into the intricate interplay between glaucoma and mental health, shedding light on the psychological toll exacted by the relentless progression of vision loss. The bidirectional relationship between glaucoma, anxiety, and depression is explored, accentuating factors like progressive vision decline and medication intricacies. Emphasizing holistic patient care, the core recommendation advocates for collaborative efforts between ophthalmologists and psychiatrists to address depression and anxiety, recognizing their impact on treatment adherence, disease trajectory, and the overall well-being of individuals grappling with glaucoma.

INTRODUCTION

Glaucoma, traditionally perceived as a progressively debilitating ocular pathology, not only encroaches upon visual acuity (VA) but also casts a profound impact on the psychological fabric of affected individuals. The relentless progression of vision loss, coupled with the constant awareness of a potentially irreversible condition, places an

immense psychological burden on patients. Recent research signifies a pivotal shift from the exclusive focus on its physical aspects to a more nuanced understanding of the psychological dimensions associated with the condition. This literature review explores the intersection of psychiatry and ophthalmology, dissecting the complexities of managing depression and anxiety in glaucoma patients. We analyze prevalence, risk factors, and mechanisms underlying mood disorders in glaucoma, unveiling the complex relationship between the conditions. Contributing factors, such as progressive vision loss and medication complexity, heighten susceptibility to mood disorders. The review explores the impact of anxiety and depression on treatment adherence, disease progression, and overall quality of life in glaucoma patients. Emphasizing holistic care, we advocate for integrated strategies involving both ophthalmologists and psychiatrists to enhance patient-centered care and quality of life.

LITERATURE REVIEW

A thorough search of the PubMed database was conducted, encompassing literature published from January 2000 to August 2023. The search utilized keywords such as "glaucoma", "depression", "anxiety", "glaucoma and depression", and "glaucoma and anxiety". The selected studies included reviews, cross-sectional, case-control, prospective, and retrospective studies, with the primary focus on investigating the correlation between glaucoma and anxiety/depression and identifying potential risk factors. To maintain stringency, case reports and meta-analyses were excluded from consideration. Only studies written in English were included in the evaluation process. The retrieved articles underwent a careful manual review to eliminate duplicates, resulting in the selection 55 articles from the screened abstracts.

PREVALENCE AND RISK FACTORS OF ANXIETY AND DEPRESSION IN GLAUCOMA

Glaucoma, characterized by the progressive loss of retinal ganglion cells (RGCs), is an optic neuropathy with no current effective treatment to control the ganglion cell

degeneration[1,2]. The management of glaucoma focuses on the proactive prevention of its progression, rendering it a chronic medical condition that necessitates lifelong care. The literature review reveals compelling evidence of a statistically significant association between glaucoma and elevated levels of anxiety and depression[3-10]. Owing to the lack of symptoms, the persisting nature of the debilitation, nature, and the looming possibility of blindness, glaucoma frequently places a psychological weight on individuals[11,12]. Individuals diagnosed with glaucoma are at an elevated risk of developing depression, a correlation substantiated by various studies. Notably, Studies from Taiwan, Japan, and Singapore collectively revealed a significant association between glaucoma and depression. In Taiwan, a retrospective cohort study involving 8777 glaucoma patients and 35108 controls showed a significantly higher hazard of depression ($P < 0.0001$)[4]. In a Japanese case-control study demonstrated elevated rates of anxiety (13.0%, $P = 0.030$) and depression (10.9%, $P = 0.026$) among 230 primary open-angle glaucoma (POAG) patients[3]. Meanwhile, in Singapore, a cross-sectional study with 15,865 glaucoma cases and 77014 controls highlighted that individuals receiving Selective Serotonin Reuptake Inhibitors had a greater risk of glaucoma incidence [odds ratio (OR): 1.39; 95% confidence interval (95%CI): 1.29-1.50][5].

In a study involving 6760 participants aged 40 years and older within the National Health and Nutrition Examination Survey, those diagnosed with glaucoma exhibited a higher prevalence of depression (10.9%, SEM: 2.20%) compared to those without glaucoma (6.9%, SEM: 0.62%). The association remained significant after adjusting for demographic factors but lost significance when considering self-reported general health[7].

Shin *et al*[6], in their retrospective case-control study spanning 2 years and involving 251 eyes diagnosed with open-angle glaucoma, observed a significant incidence of anxiety and depression in affected individuals. Similarly, Zhou *et al*[9] found high rates of anxiety and depression in Chinese glaucoma patients, with the prevalence of anxiety and depression being 22.92% and 16.40%, respectively.

Amidst the body of research on this subject, the presence of some conflicting results from studies conducted across diverse global regions introduced a layer of intricacy to the overall understanding of the subject. European cohort study published by Rezapour *et al*[13], involving 293 participants, revealed no significant association between self-reported glaucoma and depression or anxiety. The prevalence rates for depression (6.6%) and anxiety (5.3%) among individuals with glaucoma were comparable to those without glaucoma (7.7% and 6.6%). Adjusted odds ratios indicated no link between self-reported glaucoma and depression (OR: 1.10, $P = 0.80$) or anxiety (OR: 1.48, $P = 0.35$)[13]. This lack of association persisted even after adjusting for various factors, including socio-demographic variables and health parameters. Consistent with these findings, in both the Australian study by Eramudugolla *et al*[14] and the Beijing Eye Study conducted by Jonas *et al*[15], there was no evidence supporting elevated rates of depressive or anxiety symptoms associated with self-reported glaucoma. Cumurcu *et al*[16] found a correlation between pseudoexfoliative glaucoma (PXG) and depressive symptoms using assessments like the Diagnostic and Statistical Manual of Mental Disorders-IV interview, Hamilton Depression Rating Scale, Hamilton Anxiety Rating Scale, Mini Mental State Examination, and Montgomery-Asberg Depression Rating Scale. However, they noted no significant difference in anxiety levels among PXG, POAG, and control groups. In a study performed on the Israeli population, Weiss *et al*[17] discovered a depression rate in glaucoma patients similar to that of the general Israeli population, and despite depression itself not being directly linked to non-compliance, a positive correlation was observed between the severity of depression and the level of non-compliance in these patients ($P = 0.04$).

The mental health burden in glaucoma patients are influenced by various factors, including the perpetual fear of potential blindness, financial strain, and disruption to daily activities[18,19]. Insightful studies have explored nuanced risk factors for depression in glaucoma patients, such as accelerated progression of visual impairment, advanced disease stages, female gender, substance abuse, and, in some cases, advanced age[4,20]. Younger age was found to be a significant risk factor for anxiety, irrespective of

demographic and clinical variables, as indicated by a study that uncovered significant negative relationships between age and the Hospital Anxiety and Depression Scale-Anxiety (HADS-A) subscore both with (b = -0.046, P = 0.0008) and without (b = -0.043, P = 0.0022) adjusting for these factors; furthermore, older age and increasing glaucoma severity were identified as risk factors for depression in glaucoma patients[21]. In contrast, an extensive study conducted in North Carolina discovered that advanced age did not elevate the likelihood of depression[18]. Onwubiko *et al*[22] identified high rates of anxiety (44.0%) and depression (41.8%) among glaucoma patients in Enugu, Nigeria, with key contributing factors being reduced VA and also, blindness. Poor treatment adherence in glaucoma patients was associated with heightened anxiety, negatively affecting therapeutic outcomes[23]. According to the studies by Mabuchi *et al*[3] and Chen *et al*[4], the use of eye drops and the number of anti-glaucoma medications were not identified as significant risk factors for depression; furthermore, the use of topical β-blockers for glaucoma, showed no significant correlation with depression. The nature and strength of this association seemed to vary across different populations, types of glaucoma, and even treatment modalities for depression/anxiety.

THE BIDIRECTIONAL RELATIONSHIP: EXPLORING THE UNDERLYING LINK BETWEEN ANXIETY, DEPRESSION, AND GLAUCOMA

The intricate relationship between glaucoma and anxiety/depression is marked by an interplay of psychological and physiological factors. The diagnosis of chronic diseases can trigger anxiety and depression due to functional limitations, social isolation, relationship loss, guilt, and future uncertainties, while simultaneously, studies suggest that anxiety and depression can either precipitate or worsen chronic conditions[13,24-26]. The progressive vision loss and intricate medication regimens inherent in glaucoma contribute to a heightened vulnerability to mood disorders. Fear of visual deterioration becomes a continual concern. Numerous studies emphasize on the impact of glaucoma on elevating the risk of anxiety and depression[7,13,18,19]. Additionally, alternative research suggested a reciprocal relationship, revealing that a history of anxiety or

depression may increase the likelihood of developing glaucoma in individuals identified as glaucoma suspects[6,10]. In a study by Skalicky *et al*[27], a growing incidence of depression was observed as the severity of glaucoma increased. Similarly, Yochim *et al*[28] established a significant correlation between cognitive impairment, memory deficits, and mild-to-moderate depressive symptoms in a cohort of glaucoma patients. After adjusting for age, they noted that 20% of participants manifested memory impairment, while 22% exhibited compromised executive functioning, and 12.2% of individuals displayed mild-to-moderate depressive symptoms.

The interconnection between glaucoma, anxiety, and depression encompasses intricate neurobiological links that affect not only mental health but also the pathophysiological processes that influence the development and progression of this ocular condition. Studies suggest that the degeneration of retinal tissue in glaucoma is linked to an increased risk of depression and sleep disturbances[18,21,29,30]. This association may stem from disruption in the central light input and the psychological challenges posed by the chronic and progressive nature of the condition, along with the impending threat of vision loss. Glaucoma's impact on RGCs, their axons, and accompanying glial cells leads to distinct structural alterations in the optic disc and retinal nerve fiber layer (RNFL)[31]. The severity of the condition is directly correlated with a reduction in RNFL thickness[32]. The analysis of the optic nerve head (ONH) and RNFL through optical coherence tomography (OCT) is crucial for early glaucoma detection. By combining OCT with perimetry, which assesses the visual field sensitivity, clinicians can obtain a comprehensive understanding of both structural and functional aspects of the visual system. The integration of structural and functional assessments enhances the sensitivity and specificity of glaucoma diagnosis, allowing for earlier intervention and management. RNFL thickness, in particular, serves as a superior indicator compared to ONH measurements. This reflects the function of RGCs and allows for more effective monitoring of disease progression[33]. Agorastos *et al*[29] in their study, found that visual field defects (VFD) in glaucoma are pivotal predictors for depressive symptoms, trait anxiety, and sleep disturbances, with a higher prevalence of

these symptoms in severe VFD cases compared to those with minor or no VFD. The research showed that patients with severe VFD faced a significantly increased risk of achieving clinically significant psychometric scores for depression (OR: 4.0; 95%CI: 1.17-13.60), trait anxiety (OR: 6.1; 95%CI: 1.35-27.10), and sleep disturbance (OR: 4.2; 95%CI: 1.36-13.30). Ayaki *et al*[30] demonstrated that sleep disorders in glaucoma patients are associated with visual field loss and mood status, but not significantly linked to structural damage in RGCs. Additionally, Shin *et al*[6] investigated the relationship between anxiety and RNFL thinning in glaucoma patients, uncovering a significant connection with the high anxiety group exhibiting an accelerated rate of RNFL decline (P = 0.026), while no notable differences in visual field progression rates were observed between individuals with low and high anxiety or depression within the study cohort.

Intraocular pressure (IOP) is widely acknowledged as the foremost modifiable factor influencing onset or progression of glaucoma. Psychological stress has been documented to increase IOP, and this effect is mediated through the cortisol hormone, which is associated with the hypothalamic-pituitary-adrenal axis[34,35]. The autonomic nervous system (ANS) functions in regulating blood flow and IOP. The emotional responses of anxiety and depression is believed to originate in the amygdala and trigger the release of neurotransmitters and can adversely impact the ANS, stimulating multiple organs. The ANS plays a crucial role in maintaining biological balance by regulating blood flow and IOP; it is also important in the development or progression of glaucoma[36-39]. Frequent emotional fluctuations and persistent anxiety reactions can disrupt the equilibrium in the ANS, potentially exacerbating the risk of glaucoma or contributing to its progression[40]. Recognizing and addressing these multifaceted aspects, including the potential neurobiological links, is crucial for providing comprehensive support to individuals hustling through the complexities of living with glaucoma.

INTEGRATED APPROACHES TO GLAUCOMA CARE: IMPLICATIONS ON MANAGEMENT

The intersection of psychological factors, specifically anxiety and depression, with glaucoma management is integral to understanding and improving patient outcomes. The impact of these psychological elements permeates various facets of the disease trajectory, with treatment adherence serving as a focal point. Anxiety and depression may instigate hesitation, making it difficult to adhere to medication and follow-up appointments, thereby compromising the necessary steps to impede disease progression[41]. This compromised adherence becomes a gateway to exacerbated glaucomatous damage, ultimately leading to an unfavorable prognosis[42]. This progression significantly impacts the patient's overall quality of life. Detecting glaucoma in its early stages is crucial in clinical care to maintain visual function and quality of life[43,44]. Research findings indicate that simply being aware of one's glaucoma, even in the absence of visual field damage, may have a detrimental effect on the individual's quality of life[45].

The loss of peripheral visual function in glaucoma patients has cascading impact on daily activities, ranging from driving limitations, increased incidents of bumping into objects, slower walking, and a higher risk of falls. There is also a major jolt on activities like reading, which becomes evident primarily in cases of severe field damage. Although overall physical activity may not show significant difference, substantial reduction is noted with greater visual field loss[46-49]. A study by Sesar *et al*[50] asserts the negative impact of disease progression and predisposing socio-demographic factors on the quality of life in glaucoma patients. Notably, male individuals aged 50 to 69 exhibited the highest Glaucoma Health-Related Quality of Life (GHRQL), followed by those consistently using anti-glaucoma therapy and then those without glaucoma progression. These distinctions were found to be statistically significant ($P < 0.05$) based on responses to two self-administered questionnaires assessing GHRQL[50]. Ajith *et al*[51] also found elevated rates of depression (35.81%) and anxiety (25.0%) among glaucoma patients in their study, comprising 148 subjects with glaucoma and 150 subjects without glaucoma, emphasizing the need for screening protocols using Patient Health Questionnaire, the Generalized Anxiety Disorder scales. They further advocated that

the lack of ophthalmic risk factors associated with depression and anxiety accentuated the significance of psychological assessment and collaborative intervention with a psychiatrist. Social isolation, stemming from difficulties in communication and participation, adds to the emotional burden. Slota *et al*[52] stressed the importance of proactive medication concern addressal in glaucoma patients with lower health literacy, in order to enhance adherence, given by their potential reluctance to communicate issues regarding medication side effects and administration. Incorporating psychological support for severe glaucoma patients with reduced vision can enhance communication and treatment adherence[22]. Musa *et al*[53] pointed out the impact of socioeconomic barriers on glaucoma care, urging attention to factors like companionship, transportation, insurance, education, and telemedicine for improved outcomes. Additionally, addressing the stigma associated with vision loss and mental health issues, the constraint of time during medical appointments, limited access to mental health services, and the need for effective coping strategies further complicate the provision of comprehensive care. Birhan *et al*[54] conducted a cross-sectional study involving 423 glaucoma patients, revealing that 50.1% (95%CI: 45.1%-54.5%) of the surveyed individuals employed maladaptive coping strategies, potentially exacerbating mental health challenges. Conversely, Zhou *et al*[55] found a connection between improved mental health regulation and better self-management behavior in glaucoma patients in China. These studies highlight integrating coping strategy care into glaucoma treatment, to encourage positive approaches towards fostering improved overall patient well-being. To effectively address these challenges, a patient-centered approach is essential, incorporating educational initiatives that cover both the ocular and emotional aspects of glaucoma. However, recognizing the emotional toll of vision loss, the coordination of interdisciplinary collaboration among ophthalmologists, psychologists, and other healthcare professionals is crucial to ensure optimal visual outcomes while safeguarding mental and emotional well-being in the face of this challenging ocular condition.

CONCLUSION

The evidence synthesized from peer-reviewed literature reiterates the heightened susceptibility of glaucoma patients to mood disorders, attributed to factors such as progressive vision loss, complex medication regimens, and the relentless fear of visual deterioration. The bidirectional interplay between glaucoma and mood disorders, elucidated in this review, highlights the complex dynamics between ocular and emotional health. The impact of anxiety and depression on critical aspects of glaucoma care, including treatment adherence, disease progression, and overall quality of life, has been thoroughly investigated. Recognizing the psychological burden in glaucoma patients has been emphasized to be crucial for holistic and patient-centered care. Conflicting results from studies conducted across diverse global regions introduce complexity to the understanding of the subject, urging the need for further research. Future studies should aim to standardize methodologies, explore cultural and regional differences, and delve deeper into the underlying mechanisms and risk factors associated with anxiety and depression in glaucoma patients.

In conclusion, this review serves as a foundation for ongoing research endeavours to optimize the management of depression and anxiety in individuals with glaucoma. By addressing the psychological aspects of glaucoma care, healthcare providers can strive to enhance patient-centered approaches and contribute to improved outcomes for those grappling with this debilitating condition.

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Table 1 Summary of 8 selected studies on glaucoma and anxiety/depression association

Ref.	Region	Study design	No. of patient	Results	Key findings
Mabuchi *et al*[3], 2008	Japan	Case control study	230 POAG patients; 230 controls	Prevalence of anxiety: 13.0% (P = 0.030); depression: 10.9% (P = 0.026)	POAG was related to anxiety and depression
Wang *et al*[7], 2012	United States	Cross sectional study	453 glaucoma patients	10.9% prevalence of depression among self-reported glaucoma patients	Visual function parameters were associated with depression
Zhou *et al*[9], 2013	China	Cross sectional study	506 glaucoma patients	Prevalence of anxiety: 22.92%; depression: 16.40%	High anxiety and depression rates exist among Chinese glaucoma patients
Chen *et al*[5], 2017	Taiwan	Case control study	15865 glaucoma patients; 77014 controls	SSRI use linked to increased glaucoma risk (OR: 1.39, 95%CI: 1.29-1.50)	SSRIs use associated with glaucoma
Chen *et al*[4], 2018	Taiwan	Cohort study	8777 glaucoma patients; 35108 controls	In 11 yr follow up period, incidence of depression: Glaucoma group = 5.9% depression, control group = 3.2%	Patients with glaucoma are at significantly greater risk of developing depression
Berchuck *et al*[10], 2021	United States	Cohort study	3259 glaucoma suspects; 28% (911 cases) diagnosed with glaucoma during follow-up	Prevalence of anxiety: 32%; depression: 33%	Prior anxiety or anxiety with depression history raises the risk of developing glaucoma in glaucoma suspects

Shin *et al*[6], 2021	Korea	Case control study	251 eyes with POAG	Anxiety linked to disc hemorrhage, peak IOP, and RNFL thinning rate (P = 0.017, P = 0.046, P = 0.026); depression tied to visual field mean deviation and heart rate variability (P = 0.003, P = 0.006)	Anxiety increase the risk of glaucoma progression and they are also associated with IOP profile and disc hemorrhage
Dayal *et al*[8], 2022	India	Cross sectional study	200 patients	Mean HADS-anxiety = 4.5 (SD = 3.4); HADS-depression = 4.1 (SD = 3.8)	Visual loss in glaucoma correlates with anxiety and depression symptoms, regardless of disease duration

POAG: Primary open-angle glaucoma; HADS: Hospital Anxiety and Depression Scale-Anxiety; SSRI: Selective serotonin reuptake inhibitors; IOP: Intraocular pressure.

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