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DIFFERENTIAL ASSOCIATIONS OF MYOPIA WITH MAJOR AGE-RELATED EYE DISEASES : A SYSTEMATIC REVIEW

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ABSTRACT

Background: *Myopia or nearsightedness is a refractive error caused by excessive axial elongation.*

Methods: *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of cthe requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Result: *In the PubMed database, the results of our search brought up 63 articles, whereas the results of our search on SagePub brought up 21 articles. The results of the search conducted for the last year of 2013 yielded a total 44 articles for PubMed and 8 articles for SagePub. In the end, we compiled a total of 4 papers, 3 of which came from PubMed and 1 of which came from SagePub. We included five research that met the criteria.*

Conclusion: *In summary, myopic eyes are less likely to have AMD and DR but more likely to have nuclear cataract, PSC, and POAG. The associations of myopia with AMD, DR, and POAG are mostly explained by longer AL. However, the association between myopia and nuclear cataract is explained by lens refraction rather than AL.*

Keyword: *Association, Myopia, Age-Related Eye Diseas*

INTRODUCTION

Myopia is the most common clinical condition seen in our clinical practice. It is associated with various co-morbidities of the eye, which need to be evaluated at each visit. Management of myopia has witnessed revolutionary changes for two decades. Corneal topography has made our understanding of cornea more lucid and its contribution to the progression of myopia. Surgical evolution with lasers and phakic intraocular lenses has enabled patients to see spectacle-free, even with high refractive errors. This article comprehensively covers all the aspects of myopia, starting from clinical evaluation to the pros and cons of surgical treatment.[1]

The eyecare community's perspective on myopia has evolved from regarding it as a benign refractive condition to a fuller understanding of its role in eye disease and visual impairment. Myopia increases the risk of posterior subcapsular cataract, glaucoma, retinal detachment, and most importantly, myopic maculopathy (myopic macular degeneration). Furthermore, the risk of these conditions increases with each diopter of myopia. Myopia therefore increases a patient's risk of uncorrectable (nonrefractive) visual impairment in later years, with the risk again accumulating with each diopter of myopia. The management of the above diseases can be more challenging in higher levels of myopia and the outcomes are poorer.[2]

Myopia is a common refractive error affecting approximately 1.6 billion people globally.[3] Myopia or nearsightedness is a refractive error caused by excessive axial elongation. Myopia can be corrected optically by glasses, contact lenses, or refractive surgery. Nevertheless, it has been associated with complications, such as myopic macular degeneration (MMD), retinal detachment (RD), cataract, and open angle glaucoma (OAG). These complications can lead to irreversible visual impairment later in life.[4]

High myopia (spherical equivalent [SER] ≤ -6 D) is associated with reduced vision-related quality of life and has significant socioeconomic impact. The incidence of myopia and high myopia is rising globally, and it is expected that the burden of its complications will lead to considerable visual morbidity in the near future. Myopia is already the most common cause of irreversible visual impairment in the working population. A recent study estimated $6 billion global productivity loss due to MMD, and this financial burden will undoubtedly become worse in the coming decades.[4]

Worldwide, the prevalence of moderate to severe visual impairment and blindness is 285 millions, with 65% of visually impaired and 82% of all blind people being 50 years and older. Meta-analyses have shown that two out of three blind people are women, a gender discrepancy that holds true for both developed and developing countries. [5]

Cataract accounts for more than half of all blindness globally and gender inequity in access to cataract surgery is the major cause of the higher prevalence of blindness in women. In addition to gender differences in cataract surgical coverage, population-based studies on the prevalence of lens opacities indicate that women have a higher risk of developing cataract. Laboratory as well as epidemiologic studies suggest that estrogen may confer antioxidative protection against cataractogenesis, but the withdrawal effect of estrogen in menopause leads to increased risk of cataract in women.[5]

For the other major age-related eye diseases; glaucoma, age-related macular degeneration (AMD) and diabetic retinopathy, data are inconclusive. Due to anatomic factors, angle closure glaucoma is more common in women, whereas the dominating glaucoma type; primary open-angle glaucoma (POAG), is more prevalent in men. Diabetic retinopathy also has a male predominance and vascular/circulatory factors have been implied both in diabetic retinopathy and in POAG. For AMD, data on gender differences are conflicting although some studies indicate increased prevalence of drusen and neovascular AMD in women. To conclude, both biologic and socioeconomic factors must be considered when investigating causes of gender differences in the prevalence of age-related eye disease.[5]

Consistent with this trend, the prevalence of age-related conditions is also rapidly increasing. As the body ages, changes in the structural and functional characteristics of the vasculature combined with behavioral, genetic, and environmental risk factors contribute to the development of age-related vascular diseases, such as atherosclerosis, renal insufficiency, and cerebrovascular disease. Advancing age remains the strongest independent risk factor for developing atherosclerotic cardiovascular disease. Advanced age is a major risk factor for many eye diseases. The incidence and prevalence of age-related macular degeneration (AMD), glaucoma, and vascular occlusive diseases increase significantly with age. Among US adults, the prevalence of glaucoma is 0.7% among those aged 40 to 49 years and 1.8% among those aged 60 to 69 years, and increases to 7.7% for those 80 years and older. Similarly, the prevalence of AMD increases from 2.1% in the 40 to 49 year age group to 35.4% among individuals aged 80 years and above.[6]

Although the association with myopic complications has been well established, precise risk estimates of major age-related eye diseases of myopia are yet unknown.

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this literature review, we review published literature of studies to acknowledge the association of myopia and major age-related eye diseases. This is done to provide an explanation and improve the handling of treatment at the patient. As the main purpose of this paper, to show the relevance of the difficulties that have been identified as a whole.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2013, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

We used "association", "myopia" and "age-related eye disease" as keywords.The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: *(("associate"[All Fields] OR "associated"[All Fields] OR "associates"[All Fields] OR "associating"[All Fields] OR "association"[MeSH Terms] OR "association"[All Fields] OR "associations"[All Fields]) AND ("myopia"[MeSH Terms] OR "myopia"[All Fields] OR "myopias"[All Fields]) AND (("major"[All Fields] OR "majored"[All Fields] OR "majoring"[All Fields] OR "majorities"[All Fields] OR "majority"[All Fields] OR "majors"[All Fields]) AND ("agrosyst geosci environ"[Journal] OR "age"[Journal] OR "age omaha"[Journal] OR "age dordr"[Journal] OR "adv genet eng"[Journal] OR "age"[All Fields]) AND ("family"[MeSH Terms] OR "family"[All Fields] OR "relation"[All Fields] OR "relatability"[All Fields] OR "relatable"[All Fields] OR "related"[All Fields] OR "relates"[All Fields] OR "relating"[All Fields] OR "relational"[All Fields] OR "relations"[All Fields]) AND ("eye diseases"[MeSH Terms] OR ("eye"[All Fields] AND "diseases"[All Fields]) OR "eye diseases"[All Fields] OR ("eye"[All Fields] AND "disease"[All Fields]) OR "eye disease"[All Fields])))* AND *(2013:2023[pdat])* used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

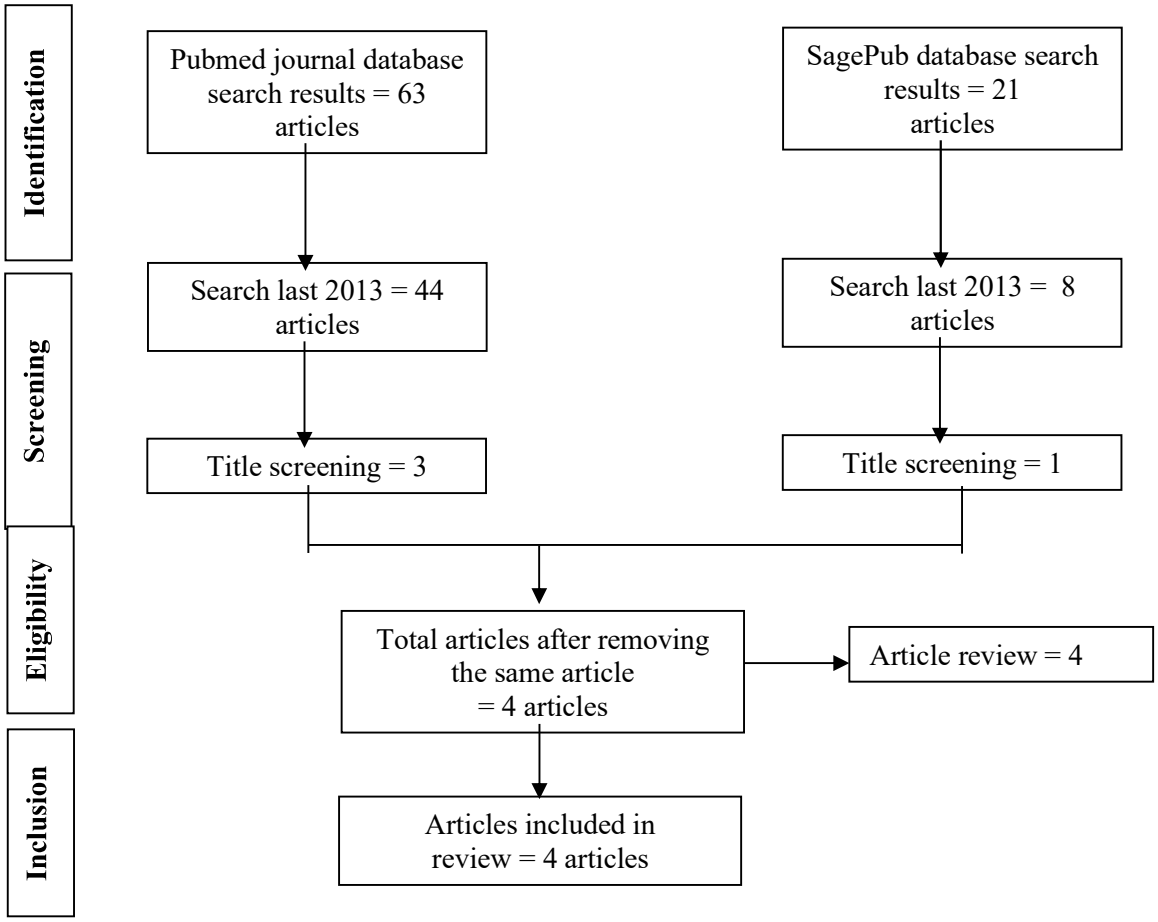

Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 63 articles, whereas the results of our search on SagePub brought up 21 articles. The results of the search conducted for the last year of 2013 yielded a total 44 articles for PubMed and 8 articles for SagePub. In the end, we compiled a total of 4 papers, 3 of which came from PubMed and 1 of which came from SagePub. We included five research that met the criteria.

Pan, et al[7] (2013) showed that myopia, but not AL, was associated with nuclear cataract, supporting the concept of index myopia with aging. Myopia, especially high myopia, may predispose to PSC cataract formation. Clinically, ophthalmologists should be aware that risk of PSC cataract appears to vary by refractive status.

Ten, et al[8] (2023) showed that high myopia is associated with diabetic retinopathy in diabetic patients. After adjustment for potential confounders, subjects with high myopia were associated with a lower risk of diabetic retinopathy.

Table 1. The litelature include in this study

Author	Origin	Method	Sample	Result
Pan et al, 2013[7]	China	Cross sectional study	3.280 patients	After excluding eyes with prior refractive or cataract surgery, 5474 eyes with gradable lens photographs were analyzed. In multivariate analyses adjusting for age, sex, body mass index, systolic blood pressure, glycosylated hemoglobin, smoking status, and education, myopia (spherical equivalent less than −0.5 diopter [D]) was associated with an increased prevalence of nuclear (OR: 4.99, 95% CI: 3.72–6.69) and PSC cataract (OR: 1.34, 95% CI: 1.30–1.39) but not with cortical cataract (OR: 0.85, 95% CI: 0.68–1.08) compared with emmetropia. Per-millimeter increase in AL was not associated with any of the three cataract subtypes. When myopia was defined as spherical equivalent of less than −5.0 D to −6.0 D, the OR of myopia for PSC cataract increased dramatically.
Ten et al, 2023[8]	China	Cross sectional study	1.317 patients	A total of 1317 participants were included in the study, including 331 participants with diabetic retinopathy, and 986 without diabetic retinopathy. After adjustment for potential confounders, subjects with high myopia were associated with a lower risk of diabetic retinopathy. The odds ratio (OR) was 0.44, 95% confidence interval (CI): (0.20–0.96), *P*-value = 0.040 in the multivariate regression analysis. Subgroup analyses showed that subjects with high myopia in the non-Hispanic Black group were associated with decreased odds of diabetic retinopathy. (OR was 0.20, and 95% CI: 0.04–0.95, *P*-value = 0.042).
Ye et al, 2022[9]	China	Cross sectional study	2.099 patients	Most participants younger than 50 years had normal vision, while the cumulative risk of VI and blindness gradually increased after 50-59 years. The percentage of each type of MM increased nonlinearly with ageing (all $p < 0.001$), with an accelerated period of increase after 45 years for MAM, and after 50 years for

				MTM and MNM. Axial length (AL) ≥30 mm was the only associated factor for mild VI or worse in participants aged 18-39 years ($p < 0.001$). Older age, AL ≥30 mm and the presence of MAM were predictors for mild VI or worse in the group aged 40-49 years (all $p < 0.05$). In participants aged ≥50 years, older age, female sex, longer AL and increased severity of MM were risk factors for VI and blindness (all $p < 0.05$).
Lee et al, 2020[3]	South Korea	Cross sectional study	17.676 patients	After adjustment for potential confounders, myopia was associated with lower risk of any age-related macular degeneration [odds ratio (OR), 0.74; 95% Confidence Interval (CI), 0.61–0.91]. In particular, myopia was significantly associated with lower odds of age-related macular degeneration in female participants (any AMD: OR, 0.71; 95% CI, 0.54–0.93; early AMD: OR, 0.70; 95% CI, 0.53–0.93) and in participants younger than 50 years (any AMD: OR, 0.46; 95% CI, 0.24–0.90; early AMD: OR, 0.47; 95% CI, 0.24–0.93). There was no significant association between myopia and age-related macular degeneration in male participants and in participants older than 50 years.

Ye, et al[9] (2022) showed that the percentages of MM and related VI increased nonlinearly with older age, with a turning point at 45 years for MAM, preceding that of MTM, MNM and VI by 5 years, warranting future longitudinal studies to confirm. Different age groups presented different risk factors for VI. Timely screening should be in place for middle-aged high myopes.

Lee, et al[3] (2020) showed that the Korean adult population, myopia was associated with significantly lower odds of any type of early age-related macular degeneration, particularly in females and in younger age group.

DISCUSSION

Refractive errors are the most frequent eye problems in all over the world. Refractive errors include myopia (near-sightedness), hyperopia (farsightedness), astigmatism (distorted vision at all distances), and presbyopia that occurs between age 40–50 years (loss of the ability to focus up close, inability to read letters of the phone book, need to hold newspaper farther away to see clearly) can be corrected by eyeglasses, contact lenses, or in some cases surgery.[10]

Myopia or nearsightedness is a refractive error caused by excessive axial elongation. Myopia can be corrected optically by glasses, contact lenses, or refractive surgery. Nevertheless, it has been associated with complications, such as myopic macular degeneration (MMD), retinal detachment (RD), cataract, and open angle glaucoma (OAG). These complications can lead to irreversible visual impairment later in life.

The most important complication of myopia is MMD, which is a common cause of visual impairment, particularly for high myopia. Characteristics of MMD are lacquer cracks, Fuchs spot, choroidal neovascularization (CNV), or chorioretinal atrophy. Posterior staphyloma is sometimes considered a specific type of MMD, whereas others consider it

rather a risk factor for developing MMD. Common peripheral retinal lesions in high myopia patients are RD, pigmentary degeneration, lattice degeneration, and pavingstone degeneration, of which RD is the most sight-threatening. For cataract, the relationship with myopia is less evident. In particular, nuclear cataract may result in a myopic shift, which hampers determination of the original refractive error. Considering OAG, Perkins et al. already published in 1982 about a higher percentage of myopic patients in the OAG population. A meta-analysis performed on 11 population-based studies also identified an increased risk of OAG for myopic persons. Whether visual field progression in myopes is similar to other OAG patients is still unclear.[11]

High myopia (spherical equivalent [SER] ≤ −6 D) is associated with reduced vision-related quality of life and has significant socioeconomic impact. The incidence of myopia and high myopia is rising globally, and it is expected that the burden of its complications will lead to considerable visual morbidity in the near future. Myopia is already the most common cause of irreversible visual impairment in the working population. A recent study estimated $6 billion global productivity loss due to MMD, and this financial burden will undoubtedly become worse in the coming decades.[11]

The classification of myopia is essential for its appropriate management. Axial myopia is the most common type observed in clinical practice and is caused by an increase in the axial length of the globe. A 1-mm increase in the axial length correlates with a myopic shift of 3 D, also known as spherical myopia. Meridional myopia, also termed myopic astigmatism, is a condition in which myopia exhibits two foci along two axes. Regular myopic astigmatism is diagnosed when the meridional difference is along the vertical and horizontal axes. Oblique astigmatism occurs when the axis is not at 90 degrees or 180 degrees. The corneal curvature, not the axial length of the globe, mostly contributes to meridional myopia. Lenticular myopia is the third most critical component of the myopic classification. The crystalline lens undergoes substantial modifications with age, eventually contributing to changes in refractive error. Thus, the lenticular component should be examined for any myopic progression in adults. The severity of myopia is categorized as mild (between −0.5 and −4 D), moderate (between −4 and −8 D), and severe (> −8 D).[12]

Macular degeneration, often called age-related macular degeneration (AMD), is an eye disorder associated with aging and results in damaging sharp and central vision. Central vision is needed for seeing objects clearly and for common daily tasks such as reading and driving. AMD affects the macula, the central part the retina that allows the eye to see fine details.[10]

Wet AMD is when abnormal blood vessel behind the retina start to grow under the macula, ultimately leading to blood and fluid leakage. Bleeding, leaking, and scarring from these blood vessels cause damage and lead to rapid central vision loss. An early symptom of wet AMD is that straight lines appear wavy. Dry AMD is when the macula thins overtime as part of aging process, gradually blurring central vision. The dry form is more common and accounts for 70–90% of cases of AMD and it progresses more slowly than the wet form. Over time, as less of the macula functions, central vision is gradually lost in the affected eye. Dry AMD generally affects both eyes. One of the most common early signs of dry AMD is drusen.[10]

Cataract is a clouding of the eye's lens and is the leading cause of blindness worldwide. Cataracts can occur at any age because of a variety of causes, and can be present at birth. Although treatment for the removal of cataract is widely available, access barriers such as insurance coverage, treatment costs, patient choice, or lack of awareness prevent many people from receiving the proper treatment.[10]

Diabetic retinopathy (DR) is a common complication of diabetes. It is characterized by progressive damage to the blood vessels of the retina, the light-sensitive tissue at the back of the eye that is necessary for good vision. DR progresses through four stages: mild nonproliferative retinopathy (microaneurysms), moderate nonproliferative retinopathy (blockage in some retinal vessels), severe nonproliferative retinopathy (more vessels are blocked leading to deprived retina from blood supply leading to growing new blood vessels), severe nonproliferative retinopathy (more vessels are blocked leading to deprived retina from blood supply leading to growing new blood vessels).[10]

Glaucoma is a group of diseases that can damage the eye's optic nerve and result in vision loss and blindness. Glaucoma occurs when the normal fluid pressure inside the eyes slowly rises. However, recent findings now show that glaucoma can occur with normal eye pressure. With early treatment, you can often protect your eyes against serious vision loss. There are two major categories "open angle" and "closed angle" glaucoma. Open angle, is a chronic condition that progress slowly over long period of time without the person noticing vision loss until the disease is very advanced, that is why it is called "sneak thief of sight." Angle closure can appear suddenly and is painful. Visual loss can progress quickly; however, the pain and discomfort lead patients to seek medical attention before permanent damage occurs.[10]

CONCLUSION

In summary, myopic eyes are less likely to have age related macular degeneration and diabetic retinopathy but more likely to have nuclear cataract, PSC, and POAG. The associations of myopia with age related macular degeneration, diabetic

retinopathy, and primary open angle glaucoma are mostly explained by longer axial length. However, the association between myopia and nuclear cataract is explained by lens refraction rather than axial length.

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