

## ASSOCIATION BETWEEN CATARACT SURGERY AND AGE-RELATED MACULAR DEGENERATION: A SYSTEMATIC REVIEW

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### Abstract

**Background:** As a leading cause of visual impairment in elderly, age-related macular degeneration has an increasing global incidence annually. It's association towards cataract surgery remains a debate.

**Aim:** The objective of this study is to summarize and evaluate the association between cataract surgery and age-related macular degeneration.

**Methods:** A systematic search strategy was conducted across several electronic reference databases (PubMed, Cochrane Library, ProQuest) and included articles published between 2018–2023. Duplicate publications, review articles, and incomplete articles were excluded.

**Results:** Databases searching identified a total of 254 articles. Of these, 29 articles passed the screening process and resulted in 12 articles for full-text assessment. The 6 articles did not evaluate the outcome of interest. Hence, we found six appropriate studies included in this review.

**Conclusion:** The results suggest that there may be an association of cataract surgery and increased risk of AMD progression and development. This association may increase according to the time of follow-up since cataract surgery. To improve medical treatment and for patients with cataract and AMD, additional research is essential to increase understanding of the disease state and its impact on AMD progression mainly prospective multicenter and RCT studies.

**Keywords:** AMD, association, cataract surgery

**INTRODUCTION**

As the foremost cause of visual impairment mainly in developed countries, age-related macular degeneration (AMD) owned the increasing global incidence. In the United States, it is estimated almost 3 million people are affected by AMD<sup>1</sup>. By 2040, the prevalence of AMD is predicted to rise to 288 million from 196 million in 2020, with Asia being the highest number of AMD patients. If remains untreated, AMD can cause further vision deterioration. For this reason, AMD is also the leading etiology of blindness for the elderly population along with cataract. The most common technique to diagnose AMD is optical coherence tomography (OCT), and now is widely used as the investigation of patients with AMD. It is critical to understand the complex interaction of factors contributing to AMD<sup>2,3</sup>. Among the debilitating factors, cataract surgery has been proposed as significantly affect AMD progression. Recently, The Age-Related Eye Disease Study (AREDS) was conducted as a multicenter randomized trial to understand the course of AMD<sup>4-7</sup>. Around 74% patients over 65 years old with visual impairment suffer from the complications of cataracts that coexist with AMD<sup>8</sup>.

Being the most common surgery performed electively worldwide, around 20 million surgeries are being done to treat cataract patients. The increasing surgeries is performed to minimalize the complication of blindness in elderly patients who are in need for vision. However, cataract surgery itself capable of surgical complications and ocular comorbidities<sup>2,9-11</sup>.

Currently, the matter of association between cataract surgery and AMD is a debate. Several studies stated that it is reasonable to deny the time of cataract surgery hence there are concerns regarding AMD exacerbation due to the inflammation in age-related cataract. However, there are also variable findings in the research. Therefore, this systematic review is intended to bring insight into the association of cataract surgery towards AMD progression for the basis of further research, treatment plan, and prevent complication.

**Method**

**Search Strategy**

This study is a qualitative systematic review. The data is obtained through electronic database search in Medline (PubMed), Scopus, Web of Science, and Google Scholar. The keywords are “Cataract Surgery” AND “Age-related macular degeneration” using English and Bahasa Indonesia. Duplicates of the articles are removed. The selected articles are based on inclusion and exclusion criteria.

**Table 1.** Literature search strategy

| Database         | Keywords                                                                                                                                                   | Results |
|------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| PubMed           | "Association" AND "cataract surgery" AND "age-related macular degeneration"<br>"Correlation" AND "cataract surgery" AND "age-related macular degeneration" | 7       |
| Cochrane Library | "Association" AND "cataract surgery" AND "age-related macular degeneration"<br>"Correlation" AND "cataract surgery" AND "age-related macular degeneration" | 6       |
| Google Scholar   | "Association" AND "cataract surgery" AND "age-related macular degeneration"<br>"Correlation" AND "cataract surgery" AND "age-related macular degeneration" | 17500   |

**Eligibility Criteria**

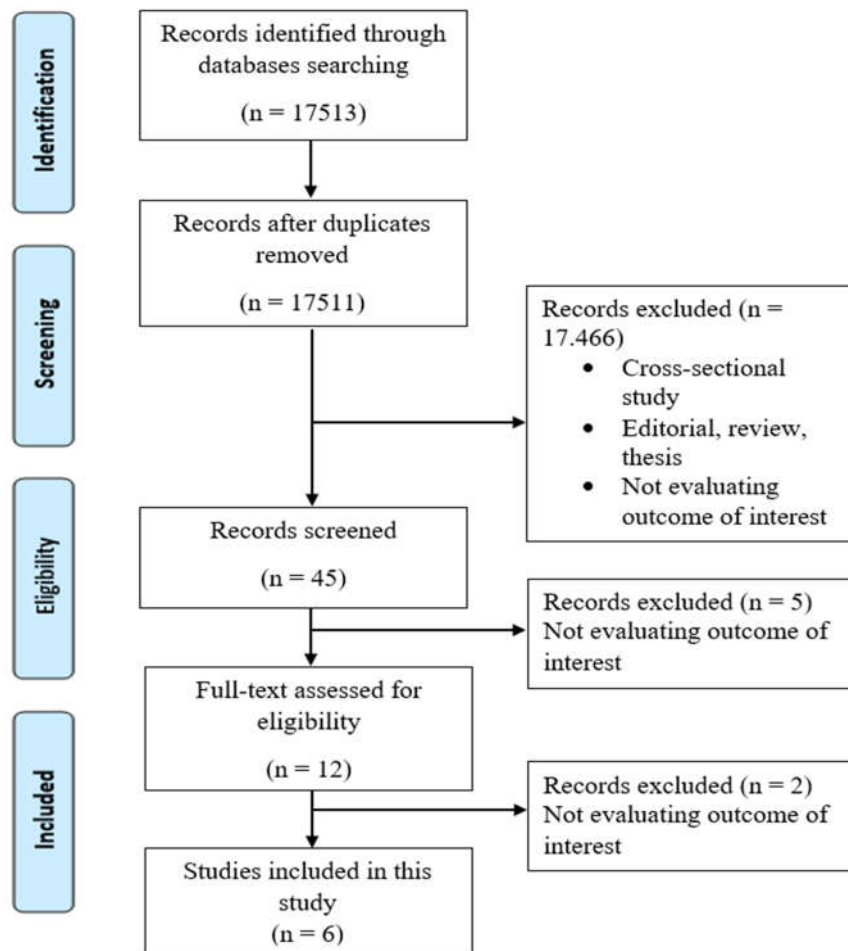
All studies were assessed for eligibility. The inclusion criteria of the included studies were articles published in the last 5 years between 2018 and 2023, full-text articles, published in Bahasa Indonesia or English, and studied the association between cataract surgery and age-related macular degeneration. The exclusion criteria of the studies are articles that are not indexed by Scopus, editorials, reviews, and articles which did not report complete data on the variables of intramedullary screw fixation. The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guideline is used for the selection. Finally, the articles are screened and synthesized into a qualitative systematic review.

**Data Extraction and Outcome**

All the authors extracted the data from the articles. Author, year of study, published year, study design, treatment, outcome, and complication of the patients in the study were identified for qualitative analysis.

**Results**

Databases searching identified a total of 17513 articles (Table 1), and they were screened based on the inclusion and exclusion criteria included in the study selection. Of these, 45 articles passed the screening process and resulted in 12 articles for full-text assessment. The six articles did not evaluate the outcome of interest. Hence, we found six appropriate studies included in this review (Figure 1). The summary of the main findings of the selected studies is presented in Table 1. Among the six studies, all of them were cohort study, with consequently prospective and retrospective. The selected studies included a total of 23611 subjects.



**Table 1.** Summary of included studies

| Author (Year)                        | Study design         | N     | Age (Years) | Follow-up (Years) | Findings                                                                                                                                                                                                                                                                                                                                                                                          |
|--------------------------------------|----------------------|-------|-------------|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Gan et al. (2020) <sup>12</sup>      | Retrospective cohort | 6790  | 55.5 ± 9.1  | 6                 | Cataract surgery may be associated with incidence of late AMD. Operated eyes had higher incidence of late AMD [1.4% vs 0.3%; adjusted risk ratio (RR): 3.47, 95% confidence interval (CI) 1.40–8.57], but not early AMD (6.0% vs 3.0%, adjusted RR: 1.12, 95% CI 0.76–1.64) or any AMD (6.9 vs 3.2%, adjusted RR: 1.23, 95% CI 0.85–1.78).                                                        |
| Bhandari et al. (2022) <sup>13</sup> | Prospective cohort   | 1767  | 50-85       | 1-12              | Cataract surgery did not increase the risk of developing late AMD with up to 10 years of follow-up (p=0.73)                                                                                                                                                                                                                                                                                       |
| Starr et al. (2018) <sup>14</sup>    | Retrospective cohort | 81    | 82.5 ± 6.1  | 0.5               | <ul style="list-style-type: none"> <li>• Significant improvement between pre- and post-operative best corrected visual acuity (BCVA) (p&lt;0.0001)</li> <li>• No significant difference in central subfield thickness before and after surgery (p&gt;0.05).</li> <li>• Cataract surgery improve the visual acuity in patients with wet AMD receiving intravitreal anti-VEGF injections</li> </ul> |
| Ho et al. (2018) <sup>15</sup>       | Prospective cohort   | 3465  | 70.2 ± 9.6  | 5                 | The incidence rate of neovascular AMD was 0.88 per 1000 person-years (95% CI: 0.66-1.14), and 1.60 (1.04-2.36) among the cataract surgery patients during a 5-year follow-up period (p<0.001)                                                                                                                                                                                                     |
| Achiron et al. (2020) <sup>16</sup>  | Retrospective cohort | 11397 | 75.4 ± 8.3  | 4                 | Patients who underwent cataract surgery using blue-light filtering intraocular lenses (BLF IOL) no difference in nAMD severity                                                                                                                                                                                                                                                                    |
| Karesvuo et al. (2021) <sup>17</sup> | Retrospective cohort | 111   | 78.9 ± 5.6  | 1                 | <ul style="list-style-type: none"> <li>• Significant decrease of central subfield macular thickness (CSMT) (p=0.001)</li> <li>• Improved visual acuity (VA) (p&lt;0.001)</li> <li>• Satisfactory visual outcomes and controlled disease activity without AMD progression</li> <li>• No evidence to delay surgery in patients who required</li> </ul>                                              |

**Discussion**

With the increasing elderly population, visual impairment is to be anticipated<sup>18</sup>. Currently, cataract surgery remains as the leading eye surgeries specifically in the aging population<sup>6,19-21</sup>. In several research, cataract surgery increased the risk of AMD progression, such as the studies by Gan et al. (2020) and Ho et al. (2018). The follow-up time is also a factor which contributes to the progression of AMD. The longer the time is, the further Although both of the research studied about the possible association between cataract surgery and AMD, other studies found that there are no significant correlation and risk<sup>22,23</sup>. A meta-analysis of AMD progression and cataract surgery has been done previously and state similarly with the follow-up of 6-10 months<sup>6,20</sup>.

The article we found in this review revealed that within up to 10 years, cataract surgery is not correlated with the severity of AMD<sup>1,2,9,10</sup>. The explanation between the association are light toxicity and phototoxic effects. The light which has short-wavelength possibly capable of reactive oxygen species liberation, thus caused the formation of protein and toxic lipid peroxidation releases. In cataract surgery, the cataract is removed thus the retina is exposed to the light, resulting in retinal damage and AMD progression. Second, the phototoxic occurrence causes dendritic cells chronic inflammation. This inflammation is also able to be induced from extracapsular extraction which leads to further AMD development. The participants possibly introduced to blue-light blocking ability lenses, as studied by Achiron et al. (2020)<sup>16</sup>. The IOLs have the possibility to prevent AMD. However, further research is still needed to examine the protective of IOLs<sup>24-26</sup>.

Other findings in the studies are cataract surgery was beneficial in the outcome of visual acuity<sup>14</sup>. The patients who initially already suffered from late AMD have better vision after cataract surgery<sup>27</sup>. This is a note for the physicians and surgeons to determine the benefits and risks in patients needing cataract surgery and suffer from AMD. Our review can also be a basis for the informed consent with patients and medical team before and after cataract surgery. It is also important to identify the risk factors of cataract surgery and AMD, as both share similar risk factors such as age, sex, ethnicity, and the signs of AMD before and after surgery<sup>10,18</sup>.

This systematic review has several limitations. First, the classification of AMD may vary between studies. Second, the study design is limited to cohort studies. However, the included articles are high-level evidence studies, hence providing reliable result.

### Conclusion

Cataract surgery may possibly associated to the development of AMD due to the light toxicity and chronic inflammation after extracapsular extraction. However, most studies found insignificant association between cataract surgery and the progression of AMD. The findings can be a basis for further studies mainly high-level evidence studies such as similar cohort or clinical trials in a different setting and specific AMD classification, thus confirm the findings.

### References

- [1]. Salimiaghdam N, Riazi-Esfahani M, Fukuhara PS, Schneider K, Kenney MC. Age-related Macular Degeneration (AMD): A Review on its Epidemiology and Risk Factors. *Open Ophthalmol J.* 2020 Jan 15;13(1):90–9.
- [2]. Grzybowski A, Kanclerz P. Recent developments in cataract surgery. In: *Current Concepts in Ophthalmology.* Springer International Publishing; 2019. p. 55–97.
- [3]. Garrigan H, Hamati J, Lalakia P, Frasso R, Salzman B, Hyman L. Does Age-Related Macular Degeneration (AMD) Treatment Influence Patient Falls and Mobility? A Systematic Review. *Ophthalmic Epidemiol.* 2022;29(2):128–38.
- [4]. Fernandes AR, Zielińska A, Sanchez-Lopez E, dos Santos T, Garcia ML, Silva AM, et al. Exudative versus Nonexudative Age-Related Macular Degeneration: Physiopathology and Treatment Options. Vol. 23, *International Journal of Molecular Sciences.* MDPI; 2022.
- [5]. Thomas CJ, Mirza RG, Gill MK. Age-Related Macular Degeneration. Vol. 105, *Medical Clinics of North America.* W.B. Saunders; 2021. p. 473–91.
- [6]. Mathis T, Kodjikian L. Age-Related Macular Degeneration: New Insights in Diagnosis, Treatment, and Prevention. Vol. 11, *Journal of Clinical Medicine.* MDPI; 2022.
- [7]. Mitchell P, Liew G, Gopinath B, Wong TY. Age-related macular degeneration. Vol. 392, *The Lancet.* Lancet Publishing Group; 2018. p. 1147–59.
- [8]. Salimiaghdam N, Riazi-Esfahani M, Fukuhara PS, Schneider K, Kenney MC. Age-related Macular Degeneration (AMD): A Review on its Epidemiology and Risk Factors. *Open Ophthalmol J.* 2020 Jan 15;13(1):90–9.
- [9]. Kim KL, Joo K, Park SJ, Park KH, Woo SJ. Progression from intermediate to neovascular age-related macular degeneration according to drusen subtypes: Bundang AMD cohort study report 3. *Acta Ophthalmol.* 2022 May 1;100(3):e710–8.
- [10]. Rossi T, Romano MR, Iannetta D, Romano V, Gualdi L, D’Agostino I, et al. Cataract surgery practice patterns worldwide: a survey. *BMJ Open Ophthalmol.* 2021 Jan;6(1):e000464.
- [11]. Surya N, Wahyudi A, Handayani N. Biometry Examination in Preparation for Cataract Surgery. 2021.
- [12]. Gan ATL, Man REK, Cheung CMG, Kumari N, Fenwick EK, Sabanayagam C, et al. Cataract surgery and the 6-year incidence of age-related macular degeneration in a multiethnic asian cohort. *Asia-Pacific Journal of Ophthalmology.* 2020;9(2):130–6.
- [13]. Bhandari S, Vitale S, Agrón E, Clemons TE, Chew EY. Cataract Surgery and the Risk of Developing Late Age-Related Macular Degeneration. *American Academy of Ophthalmology.* 2021;129(4).
- [14]. Starr MR, Mahr MA, Barkmeier AJ, Iezzi R, Smith WM, Bakri SJ. Outcomes of Cataract Surgery in Patients With Exudative Age-related Macular Degeneration and Macular Fluid. *Am J Ophthalmol.* 2018 Aug 1;192:91–7.
- [15]. Ho J der, Xirasagar S, Kao LT, Lin HC. Neovascular age-related macular degeneration is associated with cataract surgery. *Acta Ophthalmol.* 2018 Mar 1;96(2):e213–7.
- [16]. Achiron A, Elbaz U, Hecht I, Spierer O, Einan-Lifshitz A, Karesvuo P, et al. The Effect of Blue-Light Filtering Intraocular Lenses on the Development and Progression of Neovascular Age-Related Macular Degeneration. *Ophthalmology.* 2021 Mar 1;128(3):410–6.
- [17]. Karesvuo P, Elbaz U, Achiron A, Hecht I, Kaarniranta K, Tuuminen R. Effect of cataract surgery on wet age-related macular degeneration activity. *Acta Ophthalmol.* 2022 Feb 1;100(1):e262–9.

- [18]. Heloterä H, Kaarniranta K. A Linkage between Angiogenesis and Inflammation in Neovascular Age-Related Macular Degeneration. Vol. 11, Cells. MDPI; 2022.
- [19]. Zhang JH, Ramke J, Lee CN, Gordon I, Safi S, Lingham G, et al. A Systematic Review of Clinical Practice Guidelines for Cataract: Evidence to Support the Development of the WHO Package of Eye Care Interventions. Vol. 6, Vision (Switzerland). MDPI; 2022.
- [20]. Han X, Zhang J, Liu Z, Tan X, Jin G, He M, et al. Real-world visual outcomes of cataract surgery based on population-based studies: A systematic review. *British Journal of Ophthalmology*. 2022;
- [21]. Masnec S, Kalauz M. Cataract Surgery. In: *Advances in Eye Surgery* [Internet]. InTech; 2016. Available from: <http://www.intechopen.com/books/advances-in-eye-surgery/cataract-surgery>
- [22]. Alimaw YA, Hussen MS, Tefera TK, Yibekal BT. Knowledge about cataract and associated factors among adults in Gondar town, northwest Ethiopia. *PLoS One*. 2019 Apr 1;14(4).
- [23]. Jain S, Rajshekar K, Aggarwal A, Chauhan A, Gauba VK. Effects of cataract surgery and intra-ocular lens implantation on visual function and quality of life in age-related cataract patients: A systematic review protocol. *Syst Rev*. 2019 Aug 13;8(1).
- [24]. Naderi K, Gormley J, O'Brart D. Cataract surgery and dry eye disease: A review. Vol. 30, *European Journal of Ophthalmology*. SAGE Publications Ltd; 2020. p. 840–55.
- [25]. Armento A, Ueffing M, Clark SJ. The complement system in age-related macular degeneration. Vol. 78, *Cellular and Molecular Life Sciences*. Springer Science and Business Media Deutschland GmbH; 2021. p. 4487–505.
- [26]. Chakravarthy U, Bailey CC, Scanlon PH, McKibbin M, Khan RS, Mahmood S, et al. Progression from Early/Intermediate to Advanced Forms of Age-Related Macular Degeneration in a Large UK Cohort: Rates and Risk Factors. In: *Ophthalmology Retina*. Elsevier Inc.; 2020. p. 662–72.
- [27]. Galindo-Camacho RM, Blanco-Llamero C, da Ana R, Fuertes MA, Señoráns FJ, Silva AM, et al. Therapeutic Approaches for Age-Related Macular Degeneration. Vol. 23, *International Journal of Molecular Sciences*. MDPI; 2022.