

Peer-Reviewed Literature:

# Is Cataract Surgery Associated With AMD?



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Age-related macular degeneration (AMD) and cataracts are the major entities contributing to vision loss in the elderly. Previous studies<sup>1,2</sup> have shown that cataract surgery significantly improves visual function as well as quality of life in patients who have cataracts and AMD. Importantly, it has also been suggested in the literature<sup>3-9</sup> that cataract surgery may be an etiologic or exacerbating factor of AMD. This article appraises the recent studies investigating the potential link between cataract surgery and AMD. The following articles were reviewed:

1. Armbrecht AM, Findlay C, Aspinall PA, et al. Cataract surgery in patients with age-related macular degeneration: 1-year outcomes. *J Cataract Refract Surg.* 2003;29:686-693.
2. Lundstrom M, Brege KG, Floren I, et al. Cataract surgery and quality of life in patients with age-related macular degeneration. *Br J Ophthalmol.* 2002;86:1330-1335.
3. Van der Hoeve J. Senile Macula degeneration und senile Linsentrübung. *Graefes Arch Clin Exp Ophthalmol.* 1918;98:1-6.
4. Liu IY, White L, LaCroix AZ. The association of age-related macular degeneration and lens opacities in the aged. *Am J Public Health.* 1989;79:765-769.
5. Pollack A, Marcovich A, Bukelman A, et al. Age-related macular degeneration after extracapsular cataract extraction with intraocular lens implantation. *Ophthalmology.* 1996;103:1546-1554.
6. Van der Schaft TL, Mooy CM, de Bruijn WC, et al. Increased prevalence of disciform macular degeneration after cataract extraction with implantation of an intraocular lens. *Br J Ophthalmol.* 1994;78:441-445.
7. Klein R, Klein BE, Wong TY, et al. The association of cataract and cataract surgery with the long-term incidence of age-related maculopathy: the Beaver Dam Eye Study. *Arch Ophthalmol.* 2002;120:1551-1558.
8. Wang JJ, Klein R, Smith W, et al. Cataract surgery and the 5-year incidence of late-stage age-related maculopathy: pooled findings from the Beaver Dam and Blue Mountains eye studies. *Ophthalmology.* 2003;110:1960-1967.
9. Freeman EE, Munoz B, West SK, et al. Is there an association between cataract surgery and age-related macular degeneration? Data from three population-based studies. *Am J Ophthalmol.* 2003;135:849-856.
10. Klaver CC, Wolfs RC, Vingerling JR, et al. Age-specific prevalence and causes of blindness and visual impairment in an older population: the Rotterdam Study. *Arch Ophthalmol.* 1998;116:653-658.
11. Wang JJ, Mitchell PG, Cumming RG, et al. Cataract and age-related maculopathy: the Blue Mountains Eye Study. *Ophthalmic Epidemiol.* 1999;6:317-326.
12. Buch H, Vinding T, la Cour M, et al. Risk factors for age-related maculopathy in a 14-year follow-up study: the Copenhagen City Eye Study. *Acta Ophthalmol Scand.* 2005;83:409-418.
13. Cruickshanks KJ, Klein R, Klein BE, et al. Sunlight and the 5-year incidence of early age-related maculopathy: the Beaver Dam Eye Study. *Arch Ophthalmol.* 2001;119:246-250.

## INTRODUCTION

Van der Hoeve<sup>3</sup> first reported a case of AMD after cataract extraction in 1918. The association has since been noted by multiple other groups.<sup>4-6</sup> For example, the National Health and Nutrition Examination Survey<sup>4</sup> found aphakic eyes had increased odds of developing AMD compared with phakic eyes, although Pollack et al<sup>5</sup> showed in a retrospective study of patients with bilateral symmetric AMD that the progression of AMD occurred in the eye that underwent extracapsular cataract extraction. However, there have also been some studies<sup>10,11</sup> that have failed to demonstrate such an association.

## REVIEW OF THE EVIDENCE

An assessment of the literature revealed that no randomized controlled trials, meta-analyses, or systematic evaluations are available. However, several other studies have been undertaken.

The Beaver Dam Eye Study<sup>7</sup> was a prospective investigation into the risk of AMD after cataract surgery. Participants underwent baseline fundus photography and were re-examined at 5 (3,684 patients) and 10 years (2,764 patients). The incidence as well as the progression of preexisting AMD was documented. After controlling for age, gender, smoking status, alcohol consumption, and vitamin use, investigators found that participants with a history of cataract surgery prior to baseline had a significantly increased risk of AMD compared with those without such a history. At the 10-year time point, the relative risk of geographic atrophy and exudative AMD were 3.2 and 4.3, respectively. Also, cataract surgery was found to be associated with odds of 2.0 for the progression of early AMD. Unfortunately, this cohort study was neither randomized nor controlled.

Wang et al<sup>8</sup> analyzed data from the Beaver Dam Eye Study and the Blue Mountain Eye Study in an attempt to provide more definitive answers on the risk of AMD in aphakic eyes. Combining the results was possible because both studies had similar patient demographics and study designs, including fundus photography at baseline and at 5 years' follow-up as well as comparable photographic classifications of AMD. The combined data include 6,019 patients total and represent one of the largest analyses to date. The pooled data showed that, at 5 years' follow-up, more than 4% of aphakic eyes developed neovascular AMD compared with only 0.4% of phakic eyes. This difference represented a fourfold increased relative risk of neovascular AMD for nonphakic eyes. Also, nonphakic eyes were found to have odds of 5.7 for developing late-stage AMD lesions (ie, geographic atrophy or neovascular AMD).

In a similar analysis, Freeman et al<sup>9</sup> pooled data from three independent sources, the Salisbury Eye Evaluation, the Proyecto Vision Evaluation and Research Study, and the

Baltimore Eye Survey. Participants were screened at baseline for AMD using either fundus photography or clinical examination. With regression analyses, the combined results showed that cataract surgery was significantly associated with an increased risk of late-stage AMD with an odds ratio of 1.7. The interpretation of this study's results is limited, because the analyses are based on cross-sectional studies that had slightly different protocols.

Armbrecht et al<sup>1</sup> recently performed a small, prospective, nonrandomized cohort study investigating the quality of life and risk of AMD progression in a cohort of 83 patients. Subjects were divided into two groups: one underwent cataract surgery, whereas the other did not. All patients had early-stage AMD at baseline. The study demonstrated significantly improved quality-of-life indices for the cataract surgery group, with no evidence of progression of AMD at 1 year postoperatively.

A recent study by Buch et al<sup>12</sup> investigated the association of modifiable risk factors with the incidence of AMD. The cohort included 946 patients who underwent baseline fundus photography and were followed for up to 14 years. In the regression analyses, a history of cataract surgery did not emerge as a significant risk factor for the development of AMD. The interpretation of the study's results is severely limited by a very large dropout rate (fewer than 32% of subjects completed the study to final follow-up).

## INTERPRETATION OF THE LITERATURE

The current literature suggests that cataract surgery may be a predisposing factor for the development or progression of AMD. Unfortunately, the severe limitations of the available studies make it difficult to form meaningful conclusions. As no randomized trials are available, the contention that cataract surgery predisposes patients to AMD may simply be a coincidental finding derived from a discovery bias. In other words, rather than an inciting factor for AMD, cataract surgery may simply reveal preexisting AMD. For example, patients with early-stage AMD or choroidal neovascular membranes may note vision loss and seek medical attention and therefore be more likely than patients without such changes to proceed with cataract surgery. This issue was partially addressed by the Beaver Dam Eye Study,<sup>7</sup> in which patients had fundus photography at baseline to document preexisting disease. However, that study did not exclude patients with a history of AMD in their contralateral eye. Given that AMD is frequently bilateral, the eyes that underwent cataract surgery may have had early-stage AMD.<sup>8</sup> Nevertheless, as cataract surgery has emerged as a risk factor for AMD in multiple studies, a significant relationship cannot be excluded.

Despite the potential risk, ophthalmologists should continue to recommend cataract surgery to appropriate

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patients with AMD, because the procedure improves their visual function as well as quality of life.<sup>1,2</sup>

PRESUMED PATHOGENESIS

There are essentially two proposed pathophysiologic mechanisms to explain the purported relationship between cataract surgery and AMD. The first implicates photo-oxidative damage from light toxicity as the inciting agent. Phototoxicity is presumed to be a culprit in the pathogenesis of AMD, and cumulative light exposure has been associated with an increased risk of the disease.<sup>13</sup> Cataract surgery subjects the macula to potential phototoxicity intraoperatively through the operating microscope. Also, the replacement of the natural lens with an IOL may subject the retina to a lifetime of increased exposure to light of different wavelengths, particularly blue light for modern IOLs.

A second theory suggests that surgical trauma may induce inflammation that can trigger progressive AMD.<sup>6</sup> Inflammation is presumed to incite angiogenic factors that may promote neovascularization and the formation of choroidal neovascular membranes.

BOTTOM LINE

Unfortunately, the literature on the association between cataract surgery and AMD is inconsistent. As both AMD and cataracts occur in the aged and potentially share risk factors, it is difficult to comment on a definitive relationship without well-designed, randomized, controlled trials. Only with such studies can ophthalmologists confidently conclude whether an association truly exists. In the meantime, physicians should advise patients that progressive AMD is a potential risk of cataract surgery and follow patients postoperatively for the development or progression of the disease. ■

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