Surgery for cataracts in people with age-related macular degeneration

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There are no financial conflicts of interest and the authors declare that they do not have any associations with any parties who may have vested interests in the results of this review.

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Abstract

Background—Cataract and age-related macular degeneration (AMD) are common causes of decreased vision that often occur simultaneously in people over age 50. Although cataract surgery is an effective treatment for cataract-induced visual loss, some clinicians suspect that such an intervention may increase the risk of worsening of underlying AMD and thus have deleterious effects on vision.

Objectives—The objective of this review was to evaluate the effectiveness and safety of cataract surgery in eyes with AMD.

Search methods—We searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) (The Cochrane Library 2012, Issue 4), MEDLINE (January 1950 to April 2012), EMBASE (January 1980 to April 2012), Latin American and Caribbean Literature on Health Sciences (LILACS) (January 1982 to April 2012), the metaRegister of Controlled Trials (mRCT) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). There were no date or language restrictions in the electronic searches for trials. The electronic databases were last searched on 16 April 2012.

Selection criteria—we included randomized controlled trials (RCTs) and quasi-randomized trials of eyes affected by both cataract and AMD in which cataract surgery would be compared to no surgery.

Data collection and analysis—Two authors independently evaluated the search results against the inclusion and exclusion criteria. Two authors independently extracted data and assessed risk of bias for included studies. We resolved discrepancies by discussion.

Main results—One RCT with 60 participants with visually significant cataract and AMD was included in this review. Participants were randomized to immediate cataract surgery (within two weeks of enrollment) (n = 29) or delayed cataract surgery (six months after enrollment) (n = 31). At six months, four participants were lost to follow-up; two participants from each group. The immediate surgery group showed mean improvement in best-corrected visual acuity (BCVA) compared with the delayed surgery group at six months (mean difference (MD) 0.15 LogMAR, 95% confidence interval (CI) 0.28 to 0.02). There was no significant difference in the development of choroidal neovascularization between groups (1/27 eyes in the immediate surgery group versus 0/29 eyes in the delayed surgery group). Results from Impact of Vision Impairment (IVI) questionnaires suggested that the immediate surgery group fared better with quality of life outcomes than the delayed surgery group (MD in IVI logit scores 1.60, 95% CI 0.61 to 2.59). No postoperative complication was reported. We identified a second potentially relevant study of immediate versus delayed cataract surgery in 54 people with AMD. Results for the study are not yet available, but may be eligible for future updates of this review.

Authors’ conclusions—At this time, it is not possible to draw reliable conclusions from the available data to determine whether cataract surgery is beneficial or harmful in people with AMD. Physicians will have to make practice decisions based on best clinical judgment until controlled trials are conducted and their findings published.

It would be valuable for future research to investigate prospective RCTs comparing cataract surgery to no surgery in patients with AMD to better evaluate whether cataract surgery is beneficial or harmful in this group. However ethical considerations need to be addressed when delaying a potentially beneficial treatment and it may not be feasible to conduct a long-term study where surgery is withheld from the control group. Utilization of pre-existing, standardized systems for grading cataract and AMD and measuring outcomes (visual acuity, change in visual acuity, worsening of AMD and quality of life measures) should be encouraged.
Plain language summary

Cataract surgery in people with age-related macular degeneration

Cataract and age-related macular degeneration (AMD) are common causes of decreased vision that often occur simultaneously in people over age 50. Although cataract surgery is an effective treatment for cataract-induced visual loss, some clinicians suspect that such an intervention may increase the risk of worsening of underlying AMD and thus have deleterious effects on vision, mainly based on anecdotal events in which development of neovascular AMD (the ‘wet’ form) is noted in an eye soon after cataract surgery. A systematic review of the literature identified one completed randomized controlled trial (RCT) and one trial awaiting publication of results. Although data from the completed trial suggest that cataract surgery in people with AMD may improve vision without worsening of AMD, at this time it is not possible to draw reliable conclusions from the available data to determine whether cataract surgery is beneficial or harmful in people with AMD. Physicians will have to make practice decisions based on best clinical judgment until controlled trials are conducted and their findings published.

Background

Description of the condition

Age-related cataract—Cataract is an opacification of the crystalline lens that most often occurs with age (AAO 2011). According to the World Health Organization (WHO), cataract accounts for 48% of world blindness, affecting nearly 18 million people (WHO 2011). The WHO estimates that there will be 54 million people aged 60 years or older that will be blind from cataract by the year 2020, given projected increases in the elderly population in both developing and developed nations.

Age-related cataract is a term used to describe any idiopathic lens opacification that occurs in people over 50 years of age. In the early stages, symptoms may be absent or minimal, but progression of lens opacification with time generally causes varying levels of gradual, progressive, painless loss of vision. People with cataract may have increasing difficulty with near or distance vision, or both. Glare may reduce vision in bright daylight and cause trouble with night driving.

Cataract is diagnosed and assessed with a comprehensive eye exam. Reduction in best-corrected visual acuity is the standard tool used to estimate visual impairment and slit lamp biomicroscopy allows for classification and grading of the cataract. A dilated fundus examination is performed to assess for retinal disease that could complicate or exacerbate the cataract-related impairment. The American Academy of Ophthalmology recognizes the primary indication for cataract surgery as “visual function that no longer meets the affected person’s needs and for which cataract surgery provides a reasonable likelihood of improved vision” (AAO 2011). Cataract removal is also indicated when the lens opacity inhibits the proper management of posterior segment disease (AAO 2011).

Age-related macular degeneration—Age-related macular degeneration (AMD) is the leading cause of legal blindness in people 65 years or older and the incidence is expected to increase further with the continued aging of the population. In Americans 40 years or older, the total prevalence of any AMD has been estimated as 9.2% and the overall prevalence of neovascular AMD or geographic atrophy has been reported as 1.47% (EDPRG 2004; Klein 1995).

Numerous grading systems have been proposed to classify AMD but no universal consensus exists. The International Epidemiological Age-related Maculopathy Study Group defined...
age-related maculopathy (ARM) as the presence of drusen larger than 63 microns and retinal pigment epithelium abnormalities, whereas AMD was reserved for late stages of ARM with the occurrence of geographic atrophy (dry AMD) or choroidal neovascularization (CNV; wet AMD) (Bird 1995). Although neovascular disease comprises only 15% of AMD, it is responsible for the majority of visual loss (Ferris 1984).

Age-related macular degeneration may be asymptomatic in the early stages when only drusen are present (AAO 2011). Further worsening of the disease and increasing pigment alteration can be associated with a gradual visual acuity loss, diminished contrast sensitivity and a need for increased background illumination. Central geographic atrophy causes irreversible loss of central vision. Choroidal neovascularization may cause scotoma, metamorphopsia and varying degrees of loss of vision.

Although non-neovascular AMD has no treatment, high-dose vitamin supplementation was shown to reduce the incidence rate of advanced AMD (CNV or central geographic atrophy) in high-risk participants in the Age-Related Eye Disease Study ( AREDS 2001). Antioxidant vitamin and mineral supplements were shown in a systematic review to slow the progression of AMD (Evans 2006). People with CNV have been shown to benefit in large, well-designed clinical trials when treated with laser photoagulation (MPS Group 1982; MPS Group 1991), photodynamic therapy with verteporfin (TAP Study Group 1999; TAP Study Group 2001) or intravitreal pegaptanib (V.I.S.I.O.N. Clinical Trial Group 2006), ranibizumab (Brown 2006; Rosenfeld 2006), bevacizumab (CATT Research Group 2011) and aflibercept (Ohr 2012). Visual acuity may continue to decline despite appropriate treatment, however.

**Description of the intervention**

For age-related cataract, surgery is currently the only treatment option once the lens has opacified enough to cause a significant decrease in vision (AAO 2011; Ang 2012; Riaz 2006). There are four main forms of cataract extraction surgery: intracapsular (ICCE), conventional extracapsular (ECCE), extracapsular phacoemulsification and manual small incision (MSICS). Recently published Cochrane systematic reviews examined various surgical intervention techniques for eyes with age-related cataract (Ang 2012; Riaz 2006).

**How the intervention might work**

Cataract surgery in developed countries most commonly involves small-incision phacoemulsification removal of the lens and insertion of a capsule-supported intraocular lens implant. Vision-limiting operative complications are uncommon. Pooled results of cataract surgery prior to 1992 showed that 95% of participants without underlying ocular comorbidity obtained best-corrected vision of 20/40 or better (Powe 1994). When all participants were included, the probability of obtaining 20/40 or better vision was still greater than 90%. Those with underlying ocular conditions such as AMD may experience limited visual improvement. Visual outcomes for various surgical intervention techniques have been systematically reviewed (Riaz 2006).

**Why it is important to do this review**

Our understanding of the interaction of cataract and macular degeneration is still evolving. There is controversy regarding the possible benefits or risks of cataract surgery in eyes with AMD. Some studies have suggested that cataract surgery may hasten the progression of AMD (Cugati 2006; Pollack 1996), although recent reports have revealed that cataract surgery may be beneficial in this group of patients (Armbrecht 2000; Kuo 2011; Shuttleworth 1998). There are many limitations to these studies. Specifically, none of these studies involved performing fluorescein angiography immediately after surgery to permit...
determination of whether pre-existing subtle or obvious CNV or central geographic atrophy was present but not recognized prior to surgery. One prospective study in which fluorescein angiography was performed immediately prior to cataract surgery and at one week, three months and one year postoperatively found no evidence to suggest that surgery increased the risk of AMD worsening. Most cases of neovascular AMD not identified pre-operatively were believed to have been obscured by the cataract; however, this was a cohort study that did not compare surgery to no surgery (Dong 2009).

There are several scenarios in which cataract surgery might worsen the progression of AMD. Cataract and AMD share common risk factors, such as smoking and nutrition, that could cause them to progress simultaneously (Hiller 1997; Jacques 2005; Seddon 2006). In addition, inflammatory factors have been implicated in the causation of AMD (Donoso 2006) and it is feasible that inflammation occurring after cataract surgery could cause worsening of macular degeneration. Moreover, the replacement of the natural lens with an artificial lens could be associated with increased exposure to light and damaging ultraviolet rays. Clinicians who believe that cataract surgery increases the risk of AMD worsening may discourage cataract surgery despite visual loss and lens opacity. On the other hand, it could be that CNV or central geographic atrophy may be unrecognized just prior to cataract surgery and account for some of the visual loss, thus prompting an ophthalmologist to proceed with cataract surgery and then to conclude that the surgery had an effect on progression to advanced AMD when in reality the advanced stage of AMD was merely revealed by cataract surgery. This review analyzed the available evidence from randomized clinical trials regarding the effectiveness and safety of cataract surgery in eyes with AMD.

**Objectives**

The objective of this review was to evaluate the effectiveness and safety of cataract surgery in eyes with AMD.

**Methods**

Criteria for considering studies for this review

**Types of studies**—We included randomized controlled trials (RCTs) and quasi-randomized trials in which the methods of allocating people to a treatment arm were not exactly random, such as date of birth or day of the week. This was in anticipation of not finding many trials on this subject.

**Types of participants**—We included trials in eyes with AMD that also had cataract and required cataract surgery. We excluded trials in which eyes required cataract surgery for angle-closure glaucoma, lens subluxation or clear lens extraction for refractive error.

**Types of interventions**—We included trials where cataract surgery was compared to no surgery. We imposed no restrictions based on type of cataract surgery.

**Types of outcome measures**

**Primary outcomes:** The primary outcome for this review was visual acuity in the operated eye at one-year follow-up. It was measured as follows.

1. Best-corrected visual acuity dichotomized into:
   - 0.3 LogMAR (20/40 Snellen equivalent) or better;
   - worse than 0.3 LogMAR.
2. Change in visual acuity categorized by:
   - three or more lines improvement on a LogMAR chart (improvement by 0.3 LogMAR units) from baseline;
   - within three lines of baseline visual acuity;
   - loss of three or more lines of visual acuity.

When continuous LogMAR data were available we analyzed the visual acuity and degree of change as continuous data. We analyzed visual acuity at other follow-up times (six months, two and three years) when possible.

Secondary outcomes: The secondary outcomes for this review included the following.

1. Progression of AMD in the operated eye as measured by:
   - development of geographic atrophy;
   - development of CNV;
   - increase in the number of medium or large-sized drusen (> 63 microns in size);
   - increase of the drusen total area;
   - progression of non-central geographic atrophy to central geographic atrophy.

2. Vision-related quality of life as measured by methods applied in each trial.

3. Vision-threatening complications from cataract surgery, including but not limited to cystoid macular edema and retinal detachment.

We analyzed secondary outcomes at six months and one, two and three years follow-up when possible.

Search methods for identification of studies

Electronic searches—We searched the Cochrane Central Register of Controlled Trials (CENTRAL) 2012, Issue 4, part of The Cochrane Library: www.thecochranelibrary.com (accessed 16 April 2012), MEDLINE (January 1950 to April 2012), EMBASE (January 1980 to April 2012), Latin American and Caribbean Literature on Health Sciences (LILACS) (January 1982 to April 2012), the meta Register of Controlled Trials (mRCT) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). There were no language or date restrictions in the search for trials. The electronic databases were last searched on 16 April 2012.

See: Appendices for details of search strategies for CENTRAL (Appendix 1), MEDLINE (Appendix 2), EMBASE (Appendix 3), LILACS (Appendix 4), mRCT (Appendix 5), ClinicalTrials.gov (Appendix 6) and the ICTRP (Appendix 7).

Searching other resources—We searched the reference lists of included studies and related observational studies and reviews for possible trials.

Data collection and analysis

Selection of studies—Two review authors independently selected the studies for inclusion. Two authors examined the titles and abstracts of all reports identified by the
electronic and manual searching and classified each as (a) definitely include, (b) unsure or (c) definitely exclude. We obtained the full-text copies of those classified as (a) definitely include and (b) unsure. Two authors assessed each full-text copy and re-classified as (1) include, (2) awaiting assessment or (3) exclude. For studies awaiting assessment, we contacted primary investigators for further clarification and reassessed the study if further information became available. We documented studies excluded by both review authors and reported the reasons for exclusion in the review. The review authors were unmasked to the report authors, institutions and trial results during this assessment. A third review author resolved disagreements between the two review authors.

**Data extraction and management**—Two review authors independently extracted study characteristics and data for primary and secondary outcomes for the included study onto paper data extraction forms developed by the Cochrane Eyes and Vision Group. We resolved discrepancies by discussion. One review author entered data into RevMan 5 (Review Manager 2011) and a second review author verified the data entry.

**Assessment of risk of bias in included studies**—Two review authors independently assessed the included trial for bias according to the methods described in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We assessed the following parameters for risk of bias: (a) generation of random allocation sequence and allocation concealment (selection bias); (b) masking of study personnel (performance bias); (c) masking of outcome assessors (detection bias); (d) completeness of follow-up and intention-to-treat analysis (attrition bias); and (e) selective outcome reporting (reporting bias). As masking of participants is uncommon in surgical trials, we did not assess it as a measure of methodological quality.

We classified each type of bias as low risk of bias, unclear risk of bias or high risk of bias. For example, any method of allocation concealment such as sequentially numbered opaque envelopes or centralized random allocation conferred low risk of bias. When no concealment approach was reported, we considered the risk of bias to be unclear. We considered trial investigators to have conducted an intention-to-treat analysis only when all participants who were randomized, including those who were randomized but not treated, were excluded after randomization for other reasons, or were lost to follow-up, were reported and accounted for in the data analysis. When the information available in the published trial reports was inadequate to assess the risk of bias, we contacted the trial authors for clarification. If they did not respond within four weeks, we classified the trial based on the available information.

**Measures of treatment effect**—We analyzed data according to the guidelines set forth in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011). For dichotomous outcomes we calculated a risk ratio with 95% confidence intervals. We calculated a mean difference with standard deviations for continuous outcomes.

**Unit of analysis issues**—The unit of analysis was individual eyes. If both eyes from one person were included in the trial, we extracted the data and performed analyses to properly account for the non-independence of the bilateral surgery design following Chapter 9.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011).

**Dealing with missing data**—We contacted the primary investigators of included studies for additional information when statistics, such as standard deviations, or outcome data were not clearly reported or when results were not reported for all the patients who were randomized. When additional statistical information or outcome data were not provided after four weeks of contacting the primary investigators, we used the data as reported. When we
were unable to obtain results for all the patients who were randomized, we used the results reported by the authors as well as reported the loss to follow-up for each group when available.

Assessment of heterogeneity—We did not assess for heterogeneity as only one study was included in the review. If, in the future, additional studies are included in this review we will look for clinical heterogeneity by examination of the study details then test for statistical heterogeneity between trial results using the Chi$^2$ test and the I$^2$ statistic value. We will consider a P value of the Chi$^2$ test less than 0.1 or I$^2$ values of more than 50%, or both, to suggest substantial statistical heterogeneity. We also will examine the funnel plot for statistical heterogeneity if three or more studies are included.

Assessment of reporting biases—We did not assess for reporting biases as only one study was included in the review. If, in the future, additional studies are included in this review we will use asymmetry of the funnel plot as a method to identify publication bias.

Data synthesis—We did not conduct data synthesis as only one study was included in the review. If, in the future, data synthesis is possible we will combine study results when appropriate. If no substantial statistical heterogeneity is detected, and if there is no clinical heterogeneity between the trials, we will combine the results in a meta-analysis using a random-effects model. We will use a fixed-effect model if the number of trials is three or fewer. In case of substantial statistical or clinical heterogeneity we will not combine study results, but rather present a narrative or tabular summary of findings from individual trials. We will calculate a standardized mean difference if different scales are used to measure continuous outcomes.

Subgroup analysis and investigation of heterogeneity—We did not conduct subgroup analysis or investigate heterogeneity as only one study was included in the review. If, in the future, additional studies are included in this review subgroup analyses of interest will include types of cataract surgery and the presence of CNV or central geographic atrophy in the unoperated eye.

Sensitivity analysis—We did not conduct sensitivity analysis as only one study was included in the review. If, in the future, additional studies are included in this review we will conduct sensitivity analyses to determine the impact of exclusion of studies with lower methodological quality, exclusion of unpublished studies and exclusion of industry-funded studies.

Methods for future updates—We will conduct updates of this review every two years after initial publication.

Results

Description of studies

Results of the search—The original electronic searches conducted in November 2008 revealed 1184 distinct titles and abstracts of which 10 appeared potentially relevant but were excluded after further analysis. Updated searches as of April 2012 yielded 482 additional titles and abstracts. For this update, we modified the eligibility criteria for this review to include studies with less than one year of follow-up for secondary outcomes. We assessed all 1666 distinct titles and abstracts from the original and updated searches using the modified eligibility criteria and classified 19 as potentially relevant.
After full-text analysis of the 19 records, we excluded 15 records (reporting 14 studies) and did not exclude four records (reporting two studies). One study was included in the review (Lamoureux 2007) and the other study is awaiting assessment as no results have yet been published (Brunner 2001). We also identified the study awaiting assessment through a search of trial registrations on ClinicalTrials.gov (NCT01165801). We did not identify any eligible trials from searching the reference lists of possibly relevant articles. We did not conduct a comprehensive search for observational studies. Non-randomized studies and observational studies known to the authors of this review were cited in the discussion, although they were not the purpose of the systematic search.

**Included studies**—One randomized controlled trial (RCT) was included in this review (Lamoureux 2007). Of 68 eligible participants, 60 participants with visually significant cataract and AMD were enrolled in the trial. Participants were randomized to immediate cataract surgery (within two weeks of enrollment) \((n = 29)\) or delayed cataract surgery (six months after enrollment) \((n = 31)\). Six months was the typical wait time for cataract surgery at the hospital where the study was conducted, the Royal Victorian Eye and Ear Hospital in Melbourne, Australia. The trial included participants 50 years and older (range, 67 to 92). There were no statistically significant baseline imbalances reported between groups in regards to age, gender, race, risk factors for AMD or stage of AMD. At six months, four participants were lost to follow-up, two participants from each group.

**Excluded studies**—We excluded 14 studies from the review after assessment of the full text. The excluded studies and reasons for exclusion are reported in the ‘Characteristics of excluded studies’ table.

**Risk of bias in included studies**

**Allocation (selection bias)**—Methods of randomization (sequence generation) and allocation concealment were not reported in Lamoureux 2007.

**Masking (performance bias and detection bias)**—Participants randomized to either immediate surgery or delayed surgery could not be masked. It was not reported whether or not study personnel, such as operating room personnel, were masked to treatment groups. Outcome assessors were reported to be masked; however, those refracting participants and evaluating visual acuity may or may not have known whether surgery had been performed at the six-month follow-up visit. Participants were not masked when completing quality of life questionnaires.

**Incomplete outcome data (attrition bias)**—Four participants, two from each group, were lost to follow-up and not included in analysis: “One participant died, two emigrated and one refused continued participation.” The remaining 56/60 participants were analyzed in the group to which they were assigned at baseline.

**Selective reporting (reporting bias)**—No protocol was available for this trial; however, outcomes for all assessed measures were reported.

**Other potential sources of bias**—No other potential sources of bias were noted.

**Effects of interventions**

**Visual acuity (primary outcome)**—At six months, the immediate surgery group had statistically better mean best-corrected distance visual acuity (BCVA) compared with the
delayed surgery group (mean difference (MD) −0.15 LogMAR, 95% confidence interval (CI) −0.28 to −0.02).

Progression of age-related macular degeneration (AMD)—At six months, 1/27 eyes (3.7%) in the immediate surgery group developed choroidal neovascularization (CNV) compared with 0/29 eyes in the delayed (no surgery) group (risk ratio (RR) 3.21, 95% CI 0.14 to 75.68).

Quality of life—Quality of life was measured by an interviewer-administered Impact of Vision Impairment (IVI) questionnaire where participants rated items as “not at all” (0), “rarely” (1), “a little” (2), “a fair amount” (3), “a lot” (4) or “can’t do because of my eyesight” (5). Although higher scores represented poorer quality of life on the questionnaires, data were analyzed using logit units which resulted in higher mean scores representing better quality life in the analyses.

At six months, the immediate surgery group had statistically higher overall mean IVI scores compared with the delayed surgery group (MD 1.60, 95% CI 0.61 to 2.59).

Complications—Vision-threatening complications from cataract surgery were not reported by Lamoureux 2007.

Discussion

Summary of main results

The primary outcome for this review was visual acuity in the operated eye at one-year follow-up. The one study included in this review only had follow-up for six months as the control group ultimately had surgery at six months (Lamoureux 2007). At six months, greater mean best-corrected distance visual acuity (BCVA) was observed in the immediate surgery group compared with the delayed surgery control group (mean difference (MD) −0.15 LogMAR, 95% confidence interval (CI) −0.28 to −0.02). There was no significant difference in the development of choroidal neovascularization (CNV) between groups (1/27 eyes in the immediate surgery group versus 0/29 eyes in the delayed surgery group). At six months, results from Impact of Vision Impairment (IVI) questionnaires suggested that the immediate surgery group fared better with quality of life outcomes than the delayed surgery group (MD in IVI logit scores 1.60, 95% CI 0.61 to 2.59). The authors did not report adverse outcomes.

Overall completeness and applicability of evidence

The relationship between cataract surgery and age-related macular degeneration (AMD) has been the subject of much debate over recent years. Both conditions are quite common in the elderly and have overlapping symptoms, and deciding when to perform cataract surgery in patients with AMD can be difficult at best. Some clinicians believe that cataract surgery is beneficial in AMD patients whereas others fear that surgery could have deleterious effects; conflicting results from retrospective studies have led to further confusion regarding this issue (Kaiserman 2007; Sutter 2007).

This review aimed to analyze the available evidence from prospective randomized and quasi-randomized clinical trials regarding the effectiveness and safety of cataract surgery in eyes with AMD. Unfortunately, no such study with long-term follow-up (at least one year) was identified from a systematic literature search. The best available evidence from the published literature was one randomized controlled trial (RCT) with six months follow-up.
A similar study comparing immediate with delayed surgery at six months has yet to publish results (Brunner 2001).

Quality of the evidence

The Lamoureux 2007 study appeared to be well-designed; however, details for certain risk of bias domains were not reported or not clear in the published reports, such as how the allocation sequence was generated or whether allocation was concealed. Due to the nature of the surgical intervention, masking of study participants and personnel was not feasible. Outcome assessors refracting patients and evaluating visual acuity may or may not have known at six months whether surgery was performed. Further four participants, two from each group, were lost to follow-up and not included in analysis.

Potential biases in the review process

A systematic search strategy was devised to identify eligible RCTs for this review. We did not conduct a comprehensive search for observational studies. Non-randomized studies and observational studies known to the authors of this review are cited in this discussion, although they were not the purpose of the systematic search.

We contacted primary investigators of included studies for additional information not clear or not provided in their published reports. Although we received responses from investigators of both studies, not all requests for information were granted. We will update the review with information on these studies as it becomes available.

Agreements and disagreements with other studies or reviews

Evidence from non-randomized clinical trials—The best available evidence for long-term outcomes appears to be from non-randomized clinical trials and prospective observational studies (Bockelbrink 2008). Armbrecht et al performed a prospective study in which patients were grouped based on the presence or absence of AMD and cataract surgery. Three groups were comprised of (1) patients with AMD who did not have surgery, (2) patients with AMD who underwent cataract surgery, and (3) a control group of patients who underwent cataract surgery. Initial results based on five-month data suggested that cataract surgery was most beneficial for patients with moderate cataract irrespective of the degree of AMD (Armbrecht 2000). Further analysis of AMD patients found that visual acuity and quality of life benefits were maintained at one year (Armbrecht 2003). This was in contrast to previously published reports by Pollack et al, who had detected an increased rate of CNV after unilateral cataract surgery in a non-randomized trial (Pollack 1996).

Evidence from prospective cohort and case-control studies—Several well-designed epidemiologic studies have addressed the relationship amongst cataract, cataract surgery and AMD. The Copenhagen City Eye Study, the Beaver Dam Eye Study conducted in the U.S. and the Blue Mountains Eye Study conducted in Australia were large cohort studies that have addressed this issue.

The Copenhagen City Eye Study found that the presence of cataract increased the incidence of early AMD, whereas cataract surgery increased the incidence of late AMD, defined as geographic atrophy or CNV in this study (Buch 2005). Although these findings confirm that the two conditions share common risk factors, it is not possible to state whether surgery itself caused increased late AMD. Patients with neovascular AMD which was not apparent to the cataract surgeon prior to surgery may have been more likely to undergo cataract surgery because of decreasing vision before the CNV was detected.
Ten-year follow-up of the Beaver Dam Eye Study cohort found that baseline cataract was associated with early age-related maculopathy (ARM) and progression of ARM but not with late ARM (Klein 2002). Prior cataract surgery, in contrast, was associated with progression of ARM and late ARM but not with early ARM in this study. Eyes in the similarly designed Blue Mountains Eye Study had a higher 10-year risk of developing late ARM (geographic atrophy or neovascular AMD) in the presence of previous cataract surgery (Cugati 2006). In addition, analysis of combined five-year data from the Beaver Dam Eye Study and the Blue Mountains Eye Study detected an approximately 10-fold increased risk of late-stage ARM (geographic atrophy or neovascular AMD) in patients with a baseline history of prior cataract surgery (Wang 2003). It was not possible to determine the presence of a cause-and-effect relationship between cataract surgery and progression of ARM or the presence of late ARM from a cohort study, and further study is needed to clarify this issue.

A case-control study within AREDS found an increased risk of lens opacities or cataract surgery in participants with large drusen and in participants with neovascular AMD (AREDS 2000). There was no association between lens opacities or previous cataract surgery and geographic atrophy in this study. A more recent AREDS report addressing the risk of developing advanced AMD (as seen on annual fundus photographs) after cataract surgery found no clear effect of cataract surgery on the risk of progression (Chew 2009). A previous publication on a Chesapeake Bay waterman cohort, interestingly, had detected a higher incidence of AMD in the presence of nuclear (but not cortical) opacity (West 1989).

Authors’ conclusions

Implications for practice

At this time, it is not possible to draw reliable conclusions from the available data to determine whether cataract surgery is beneficial or harmful in people with age-related macular degeneration (AMD). Physicians will have to make practice decisions based on best clinical judgment until appropriate studies with long-term follow-up are conducted and reported.

Implications for research

It would be valuable for clinical researchers to design prospective randomized controlled trials (RCTs) comparing cataract surgery to no surgery in patients with AMD to better evaluate whether cataract surgery is beneficial or harmful in this group. However ethical considerations need to be addressed when delaying a potentially beneficial treatment and it may not be feasible to conduct a long-term study where surgery is withheld from the control group. Utilization of pre-existing, standardized systems for grading cataract and AMD and measuring outcomes (visual acuity, change in visual acuity, worsening of AMD and quality of life measures) should be encouraged.

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Sources of support
References to studies

Included studies


Excluded studies


Studies awaiting classification


Other references

Additional references


Evans 2006. Evans JR. Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration. Cochrane Database of Systematic Reviews. 2006; (2):Art. No.: CD000254.10.1002/14651858.CD000254.pub2


Cochrane Database Syst Rev. Author manuscript; available in PMC 2013 June 13.
Other published versions of this review


Appendices

1 CENTRAL search strategy

#1 MeSH descriptor Retinal Degeneration
#2 MeSH descriptor Retinal Neovascularization
#3 MeSH descriptor Choroidal Neovascularization
#4 MeSH descriptor Macula Lutea
#5 maculopath*
#6 macula* or retina* or choroid* near degener*
#7 macula* or retina* or choroid* near neovasc*
#8 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)
#9 MeSH descriptor Cataract explode all trees
#10 MeSH descriptor Cataract Extraction explode all trees
#11 cataract* near/4 (extract* or aspirat* or operat* or remov* or surg* or excis* or implant*)
#12 lens* near/4 (extract* or aspirat* or operat* or remov* or surg* or excis* or implant*)
#13 phacoemulsif* or capsulorhexis or lensectomy
#14 (#9 OR #10 OR #11 OR #12 OR #13)
#15 (#8 AND #14)

2 MEDLINE (OvidSP) search strategy

1. randomized controlled trial.pt.
2. (randomized or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1–7
9. exp animals/
10. exp humans/
11. 9 not (9 and 10)
12. 8 not 11
13. exp retinal degeneration/
14. retinal neovascularization/
15. choroidal neovascularization/
16. exp macula lutea/
17. maculopath$.tw.
18. ((macul$ or retina$ or choroid$) adj3 degener$).tw.
19. ((macul$ or retina$ or choroid$) adj3 neovasc$).tw.
20. or/13–19
21. exp cataract/
22. exp cataract extraction/
23. ((extract$ or aspirat$ or operat$ or remov$ or surg$ or excis$ or implant$) adj3 cataract$).tw.
24. ((extract$ or aspirat$ or operat$ or remov$ or surg$ or excis$ or implant$) adj3 lens$).tw.
25. (pha?oemulsif$ or capsulorhexis or lensectomy).tw.
26. or/21–25
27. 20 and 26
28. 12 and 20 and 27

The search filter for trials at the beginning of the MEDLINE strategy is from the published paper by Glanville (Glanville 2006).

3 EMBASE (OvidSP) search strategy

1. exp randomized controlled trial/
2. exp randomization/
3. exp double blind procedure/
4. exp single blind procedure/
5. random$.tw.
6. or/1–5
7. (animal or animal experiment).sh.
8. human.sh.
9. 7 and 8
10. 7 not 9
11. 6 not 10
12. exp clinical trial/
14. ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).tw.
15. exp placebo/
16. placebo$.tw.
17. random$.tw.
18. exp experimental design/
19. exp crossover procedure/
20. exp control group/
21. exp latin square design/
22. or/12–21
23. 22 not 10
24. 23 not 11
25. exp comparative study/
26. exp evaluation/
27. exp prospective study/
28. (control$ or prospectiv$ or volunteer$).tw.
29. or/25–28
30. 29 not 10
31. 30 not (11 or 23)
32. 11 or 24 or 31
33. exp retina degeneration/
34. retina neovascularization/
35. subretinal neovascularization/
36. exp retina macula lutea/
37. maculopath$.tw.
38. ((macul$ or retina$ or choroid$) adj3 degener$).tw.
39. ((macul$ or retina$ or choroid$) adj3 neovasc$).tw.
40. or/33–39
41. exp cataract/
42. exp cataract extraction/
43. ((extract$ or aspirat$ or operat$ or remov$ or surg$ or excis$ or implant$) adj3 cataract$).tw.
44. ((extract$ or aspirat$ or operat$ or remov$ or surg$ or excis$ or implant$) adj3 lens$).tw.
45. (pha?oemulsif$ or capsulorhexis or lensectomy).tw.
46. or/41–45
47. 40 and 46
48. 32 and 47
4 LILACS search strategy
   cataract$ and macula$ degenerat$ or AMD or ARMD

5 metaRegister of Controlled Trials search strategy
   (macular degeneration) AND (cataract)

6 ClinicalTrials.gov search strategy
   (Macular Degeneration or AMD or ARMD) AND Cataract

7 ICTRP search strategy
   age related macular degeneration AND cataract