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Surgery for cataracts in people with age-related macular degeneration

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*Indicates the major publication for the study

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Designing the review: HC
Co-ordinating the review: HC
Data collection for the review

- Designing search strategies: Iris Gordon, HC
- Undertaking searches: Iris Gordon
- Screening search results: HC, NB, KL
- Organizing retrieval of papers: HC, KL
- Screening retrieved papers against inclusion criteria: HC, NB, KL
- Appraising quality of papers: HC, NB
- Extracting data from papers: HC, NB
- Writing to authors of papers for additional information: HC
- Providing additional data about papers: HC
- Obtaining and screening data on unpublished studies: HC, NB

Data management for the review

- Entering data into RevMan: HC, KL

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Abstract

Background—Cataract and age-related macular degeneration (AMD) are significant causes of decreased vision in the elderly that often occur simultaneously. Although cataract surgery is an effective treatment for cataract-induced visual loss, some clinicians suspect that such an intervention may increase the risk of progression 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 strategy—We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Group Trials Register) (*The Cochrane Library*, Issue 4, 2008), MEDLINE (January 1966 to November 2008), EMBASE (January 1980 to November 2008) and Latin American and Caribbean Literature on Health Sciences (LILACS) (January 1982 to November 2008). There were no language or date restrictions in the search for trials. The electronic databases were last searched on 4 November 2008.

Selection criteria—We planned to include 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. Discrepancies were resolved by discussion.

Main results—We found no RCTs, thus no analysis was conducted. Evidence was limited to non-randomized clinical trials and prospective cohort and case-control studies.

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 judgement until controlled trials are conducted and their findings published.

Medical Subject Headings (MeSH)

Cataract [*complications]; Cataract Extraction [*adverse effects]; Disease Progression; Macular Degeneration [complications; *pathology]

MeSH check words

Humans

Background

Description of the condition

Age-related cataract—Cataract is an opacification of the crystalline lens that most often occurs with age (AAO 2006). According to the World Health Organization (WHO), cataract accounts for 48% of world blindness, affecting nearly 17.6 million people (WHO 2004). With projected increases in the elderly population taken into consideration for both

developing and developed nations, 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.

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 2006). Cataract removal is also indicated when the lens opacity inhibits the proper management of posterior segment disease (AAO 2006).

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 2006). Further progression 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.

Non-neovascular AMD has no treatment but 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 randomized clinical trials when treated with laser photocoagulation (MPS Group 1982; MPS Group 1991), photodynamic therapy with verteporfin (TAP Study Group 1999; TAP Study Group 2001), or anti-angiogenic agents using pegaptanib (V.I.S.I.O.N. Clinical Trial Group 2006) or ranibizumab Brown 2006; Rosenfeld 2006), depending on the clinical situation. 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 2006; Riaz 2006). There are four main forms of cataract extraction surgery: intracapsular (ICCE), traditional extracapsular (ECCE), phacoemulsification, and manual small incision (MSICS). One recent published Cochrane systematic review examined various surgical interventions for eyes with age-related cataract (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 two recent reports have revealed that cataract surgery may be beneficial in this group of patients (Armbrecht 2000; Shuttleworth 1998). There are many limitations to these studies. Specifically, no study to date performed 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.

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 progression 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 progression

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 vision 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 merely was revealed by cataract surgery. This review will analyze 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 to be measured as:

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;
    - Three or more lines loss.

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

Secondary outcomes: The secondary outcomes for this review included:

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 planned to analyze secondary outcomes at one, two, three years follow-up when possible.

Search methods for identification of studies

Electronic searches—We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Group Trials Register) (*The Cochrane Library*, Issue 4, 2008), MEDLINE (January 1966 to November 2008), EMBASE (January 1980 to November 2008) and Latin American and Caribbean Literature on Health Sciences (LILACS) (January 1982 to November 2008). There were no language or date restrictions in the search for trials. The electronic databases were last searched on 4 November 2008.

See: Appendices for details of search strategies for CENTRAL (Appendix 1), MEDLINE (Appendix 2), EMBASE (Appendix 3) and LILACS (Appendix 5).

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

Data collection and analysis

Selection of studies—Two review authors independently selected the studies for inclusion. The titles and abstracts of all reports identified by the electronic and manual searching were examined by two authors. The abstracts were classified as (a) definitely include, (b) unsure or (c) definitely exclude. Full-text copies of those classified as (a) definitely include and (b) unsure were obtained and re-assessed by two authors. The studies were classified as (1) include, (2) awaiting assessment or (3) exclude. For studies awaiting

assessment, study authors were contacted for further clarification and the study was reassessed if further information became available. Studies excluded by both review authors are documented and the reasons for exclusion are reported in the review. The review authors were unmasked to the report authors, institutions and trial results during this assessment. Disagreements between the two review authors were resolved by a third review author.

Data extraction and management—There were no studies included in the review; therefore no data extraction was performed. In the future, for studies that meet the inclusion criteria for this review, two review authors will independently extract the data for the primary and secondary outcomes onto paper data extraction forms developed by the Cochrane Eyes and Vision Group. A pilot test of this form will be done using a small number of studies. Discrepancies will be resolved by discussion. After the data extraction is verified, all data will be entered into RevMan 5 (RevMan 2008).

Assessment of risk of bias in included studies—There were no studies included in the review; therefore no assessment of methodological quality was performed. In the future, if studies meet the inclusion criteria for this review, two review authors will independently assess the included trials for bias according to the methods described in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008). The following parameters will be assessed for bias: (a) generation of random allocation sequence and allocation concealment (selection bias); (b) masking study personnel (performance bias); (c) completeness of follow up and intent-to-treat analysis (attrition bias); (d) masking of outcome assessors (detection bias); and (e) selective outcome reporting (reporting bias). As masking of participants is uncommon in surgical trials, it will not be assessed as a measure of methodological quality.

Each type of bias will be classified as low risk of bias, unclear risk of bias, or high risk of bias. Any method of allocation concealment such as sequentially numbered opaque envelopes or centralized random allocation will be considered to confer low risk of bias. If the information available in the published trial reports is inadequate to assess the method of allocation concealment, we will contact the trial authors for clarification. If they do not respond within four weeks time, we will classify the trial based on the available information. When studies do not report any concealment approach, risk of bias will be considered unclear. We will also assess the impact of any assumptions made in this regard in a sensitivity analysis.

We will consider trial investigators to have conducted an intent-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.

Measures of treatment effect—We will analyze data according to the guidelines set forth in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2008). For dichotomous outcomes we will calculate a summary risk ratio with 95% confidence intervals. We will also report the risk difference and number needed to treat. We will calculate a mean difference with standard deviations for continuous outcomes. We will

calculate a standardized mean difference if different scales are used to measure continuous outcomes.

Unit of analysis issues—The unit of analysis will be individual eyes. If both eyes from one person were included in the trial, we will extract the data and perform 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 2008).

Dealing with missing data—We will contact the authors of included studies for additional information when statistics, such as standard deviations, or outcome data are not clearly reported or if results are not reported for all the patients who were randomized. If additional statistical information or outcome data cannot be provided, we will use data as it is reported. If we are unable to obtain results for all the patients who were randomized, we will use the results reported by the authors as well as report the loss to follow-up for each group when available.

Assessment of heterogeneity—We will look for clinical heterogeneity by examination of the study details then test for statistical heterogeneity between trial results using the Chi-square test and the I-square value. A p value of the Chi-square test less than 0.1 or I-square values of more than 50% or both will be considered to suggest substantial statistical heterogeneity. We will also examine the funnel plot for statistical heterogeneity if three or more studies are included.

Assessment of reporting biases—Asymmetry of the funnel plot will be used to identify publication bias.

Data synthesis—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. A fixed-effect model will be used if the number of trials is three or less. 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.

Subgroup analysis and investigation of heterogeneity—Subgroup analyses of interest include types of cataract surgery and the presence of CNV or central geographic atrophy in the unoperated eye.

Sensitivity analysis—Sensitivity analyses will be conducted 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: Updates of this review will be conducted every two years after initial publication.

Results

Description of studies

See: Characteristics of excluded studies.

The electronic searches revealed 1,183 distinct titles and abstracts of which 10 appeared potentially relevant but were excluded after further analysis. 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 not the purpose of the systematic search.

Risk of bias in included studies

There were no RCTs or quasi-randomized trials identified; therefore no assessment of risk of bias was performed.

Effects of interventions

There were no RCTs or quasi-randomized trials identified; therefore no effects of interventions are reported.

Discussion

The relationship between cataract surgery and 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 and 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 was identified from a systematic literature search. The best available evidence from the published literature appeared to be from non-randomized clinical trials and prospective observational studies (Bockelbrink 2008).

Evidence from non-randomized clinical trials

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 between 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 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 (geographicatrophy 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 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 AMD. Physicians will have to make practice decisions based on best clinical judgement until appropriate studies are conducted and reported.

Implications for research

It would be valuable for clinical researchers to design 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. Utilization of pre-existing, standardized systems for grading cataract and AMD and measuring outcomes (visual acuity, change in visual acuity, progression of AMD, and quality-of-life measures) should be encouraged.

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Internal sources

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External sources

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Characteristics of Studies

Characteristics of included studies *[ordered by study ID]*

Armbrecht 2000	Prospective cohort study 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.
Armbrecht 2003	Prospective cohort study comprised of (1) patients with AMD scheduled to have cataract surgery and (2) a control group of patients with AMD not having cataract surgery.
Brunner 2001	RCT with two arms: Group 1 = Immediate cataract operation (only one eye per patient); Group 2 = Control group with 6-month presurgical observation and postsurgical observation 1 week after operation (likewise only one eye per patient). This study was excluded since the timing of cataract surgery was not the intervention of interest for this review.
Javitt 2000	Case series of patients undergoing cataract surgery.
Lamoureux 2007	RCT with two arms: “early surgery” versus “standard surgery” for patients with AMD scheduled for cataract surgery. This study was excluded since the timing of cataract surgery was not the intervention of interest for this review.
Lundström 2002	Prospective cohort study of patients undergoing cataract surgery, with and without AMD.
Pollack 1996	Observational study of eyes with AMD that had cataract surgery, compared to fellow eyes that did not have surgery.
Pollack 1998	Observational study of patients with AMD after cataract surgery in 1st eye, then 2nd eye.
Prajna 1998	Study was not limited to patients with AMD.

AMD: age-related macular degeneration

RCT: randomized clinical trial

Data and Analyses

This review has no analyses.

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor Macular Degeneration

#2 MeSH descriptor Retinal Degeneration

#3 MeSH descriptor Retinal Neovascularization

#4 MeSH descriptor Choroidal Neovascularization

#5 MeSH descriptor Macula Lutea

#6 maculopath*

#7 macula* or retina* or choroid* near degener*

#8 macula* or retina* or choroid* near neovasc*

#9 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8)

#10 MeSH descriptor Cataract

#11 MeSH descriptor Cataract Extraction

#12 MeSH descriptor Capsulorhexis

#13 MeSH descriptor Phacoemulsification

#14 cataract* near/4 (extract* or aspirat* or operat* or remov* or surg* or excis* or implant*)

#15 lens* near/4 (extract* or aspirat* or operat* or remov* or surg* or excis* or implant*)

#16 phacoemulsif*

#17 lensectomy

#18 (#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17)

#19 (#9 AND #18)

Appendix 2. MEDLINE 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 macular degeneration/
14. exp retinal degeneration/
15. exp retinal neovascularization/
16. exp choroidal neovascularization/
17. exp macula lutea/
18. maculopath$.tw.
19. ((macul$ or retina$ or choroid$) adj3 degener$).tw.
20. ((macul$ or retina$ or choroid$) adj3 neovasc$).tw.
21. or/13-20
22. exp cataract/
23. exp cataract extraction/
24. exp capsulorhexis/
25. exp phacoemulsification/
26. ((extract$ or aspirat$ or operat$ or remov$ or surg$ or excis$ or implant$) adj3 cataract$).tw.
27. ((extract$ or aspirat$ or operat$ or remov$ or surg$ or excis$ or implant$) adj3 lens$).tw.
28. pha?oemulsif$.tw.
29. lensectomy.tw.
30. or/22-29
31. 21 and 30
32. 12 and 31

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

Appendix 3. EMBASE search strategy

1. exp randomized controlled trial/
2. exp randomization/
3. exp double blind procedure/

4. exp single blind procedure/
5. random$.tw.
6. or/1-5
7. (animal or animal experiment).sh.
8. human.sh.
9. 7 and 8
10. 7 not 9
11. 6 not 10
12. exp clinical trial/
13. (clin$ adj3 trial$).tw.
14. ((singl$ 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 macula degeneration/
34. exp retina degeneration/
35. exp retina neovascularization/

36. exp subretinal neovascularization/
37. exp retina macula lutea/
38. maculopath$.tw.
39. ((macul$ or retina$ or choroid$) adj3 degener$).tw.
40. ((macul$ or retina$ or choroid$) adj3 neovasc$).tw.
41. or/33-40
42. exp cataract/
43. exp cataract extraction/
44. exp capsulorhexis/
45. exp phacoemulsification/
46. ((extract$ or aspirat$ or operat$ or remov$ or surg$ or excis$ or implant$) adj3 cataract$).tw.
47. ((extract$ or aspirat$ or operat$ or remov$ or surg$ or excis$ or implant$) adj3 lens$).tw.
48. pha?oemulsif$.tw.
49. lensectomy.tw.
50. or/42-49
51. 41 and 50
52. 32 and 51

Appendix 4. LILACS search terms

cataract$ and macula$

References to studies excluded from this review

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Plain Language Summary

Cataract surgery in people with age-related macular degeneration

Cataract and age-related macular degeneration (AMD) are significant causes of decreased vision in the elderly that often occur simultaneously. Although cataract surgery is an effective treatment for cataract-induced visual loss, some clinicians suspect that such an intervention may increase the risk of progression of underlying AMD and thus have deleterious effects on vision. 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 judgement until controlled trials are conducted and their findings published.