Diabetic-retinopathy progression following phacoemulsification

A metaanalysis

ABSTRACT

Purpose
To determine the effect of phacoemulsification on the progression of diabetic retinopathy.

Methods
We conducted an electronic search of the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Group Trials Register) on *The Cochrane Library* (Issue 1, 2005), MEDLINE, and the reference lists of identified trials evaluating the effects of phacoemulsification on the progression of diabetic retinopathy. There were no language or date restrictions in the electronic search. Two reviewers independently assessed the articles for inclusion. Odds ratio at 95% confidence interval was determined using Review Manager 4.2.2 (The Cochrane Collaboration, Oxford, United Kingdom).

Results
No randomized controlled trials were found. Five nonrandomized, prospective, case-controlled trials involving a total of 804 eyes were included in this review. All 5 trials studied the effects of phacoemulsification on the progression of diabetic retinopathy using the fellow nonoperated eye as control. Pooled analysis showed weak evidence to support the progression of diabetic retinopathy (RR=1.36: 95%; CI 0.95-1.96) in eyes that underwent phacoemulsification compared with eyes that did not.

Conclusion
The available literature consists mainly of retrospective case reviews and case-controlled trials that are difficult to compare and analyze due to variations in the definition of progression and retinopathy assessment and surgical technique. However, the 5 studies reviewed show that uncomplicated phacoemulsification had minimal or no effect on the progression of diabetic retinopathy. Further randomized, controlled trials are needed to confirm this finding.

Keywords: Metaanalysis, diabetic retinopathy, cataract extraction, phacoemulsification
The global prevalence of diabetes is increasing rapidly, estimated at 110 million in 1994 and projected to reach 221 million by 2010. The risk of developing a visually significant cataract is significantly increased in diabetic patients, in whom surgical management is disproportionately more problematic compared with nondiabetic patients. Both the postoperative progression of diabetic retinopathy and macular edema are considered common causes of poor visual acuity in diabetic patients after uncomplicated cataract surgery, and whether these represent the natural course of the disease or are direct effects of the surgery is still uncertain.

Cataract surgery in diabetic patients has been marked with a high incidence of intraoperative and postoperative complications, which have been implicated in postoperative progression of diabetic retinopathy. Studies point to retinopathy severity and macular edema as the principal determinants of postoperative visual acuity, and link improved visual outcomes to the shift from conservative management to earlier surgical intervention.

The degree of diabetic retinopathy has been correlated with visual outcome in a metaanalysis of extracapsular cataract extractions (ECCE) that analyzed proportions of eyes achieving 20/40 or better central acuity. Earlier cataract extraction in diabetic patients has been proposed to improve visualization and monitoring of the fundus, which would allow prompt treatment and increase long-term visual outcome. Postoperative progression has also been related to the presence and stage of retinopathy at baseline. However, the postulated risk factors have not been consistent; the presence of background retinopathy has been implicated in some reports and active proliferative retinopathy in others. A more favorable visual outcome has been observed with preoperative treatment of retinopathy when indicated and the use of newer, small-incision cataract-surgery techniques such as phacoemulsification.

An evidence-based approach to the practice of medicine is becoming more important in the face of increasing pressure on health-care professionals to deliver quality and cost-effective care. The decision to surgically remove cataracts in patients with diabetic retinopathy to improve visualization of the fundus and allow monitoring and treatment must outweigh the risk of possible progression of the retinopathy. The conflicting conclusions in studies investigating the progression of diabetic retinopathy after phacoemulsification prompt a systematic review of the best available evidence on the effect of phacoemulsification on the postoperative progression of diabetic retinopathy.

This review was done to determine the effect of phacoemulsification on the progression of diabetic retinopathy.

**METHODOLOGY**

**Criteria for inclusion of studies in this review**

**Types of studies.** This review intended to include randomized controlled trials. However, none was found, and the results of 5 prospective, case-controlled trials comparing the progression of diabetic retinopathy after phacoemulsification versus no surgery were included.

**Types of participants.** Study participants were patients diagnosed clinically with diabetes mellitus who have undergone phacoemulsification in 1 eye and no surgery in the fellow eye.

**Types of interventions.** Unilateral phacoemulsification and implantation of an intraocular lens compared with no surgery in the fellow eye among diabetic patients.

**Types of outcome measures.** The primary outcome measure was the occurrence or progression of any type of diabetic retinopathy for at least 6 months following phacoemulsification.

**Search strategy for identification of studies**

Two independent searches of PubMed and Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Group trials register) on The Cochrane Library (Issue 1, 2005) were conducted to identify all published articles on the progression of diabetic retinopathy following phacoemulsification. Clinical queries focusing on phacoemulsification, cataract surgery, and diabetic retinopathy were used to provide a broad search of all available clinical trials. There were no date or language restrictions in the electronic searches. Manual searches of the reference lists of included studies, other reviews, and book chapters on surgery for cataracts and diabetic retinopathy to find additional trials were conducted. Trial investigators and experts in the field were contacted to identify additional published and unpublished studies. Manual searches of journals or conference proceedings were not done.

**Methods of the review**

**Selection of trials.** Two reviewers independently assessed the titles and abstracts resulting from the electronic searches. Full copies of potentially relevant reports were obtained. No studies fulfilled the criteria for randomized, controlled trials. We then proceeded to look for other types of studies pertinent to our search queries.

**Assessment of methodological quality.** Assessment of methodological quality was based on the methods in section 6 of the Cochrane Reviewers’ Handbook. Four parameters were considered:
1. Allocation concealment and method of allocation to treatment
2. Masking of providers and recipients of care
3. Masking of outcome assessment
4. Completeness of follow-up.
   Each parameter was graded as follows: A = adequate, B = unclear, or C = inadequate.

**Data extraction and synthesis.** Data from studies were summarized collecting similar outcomes and using similar follow-up times after testing for heterogeneity between trial results using a standard chi-square test. For dichotomous data, results were expressed as odds-ratio estimates (95% confidence interval). For continuous data, the mean and standard deviations were obtained. Standard errors were converted to standard deviations and summarized as weighted mean differences (95% confidence intervals).

**Description of studies**

The electronic searches identified 49 reports of studies on progression of diabetic retinopathy after cataract surgery. There were no randomized controlled clinical trials assessing the progression of diabetic retinopathy after phacoemulsification. Five nonrandomized, prospective, case-controlled studies of similar study design were identified as follows:

- Squirrell D, Bhola R, Bush J, Winder S, Tabot JF. A prospective, case-controlled study of the natural history of diabetic retinopathy and maculopathy after uncompli-

**Methodological quality**

No assessment of quality was undertaken for the 5 prospective nonrandomized, case-controlled studies because they were different in study design from the criteria set in the *Cochrane Reviewers’ Handbook*. All 5 studies investigated the effect of the progression of diabetic retinopathy among patients undergoing monocular phacoemulsification using the fellow eye as control. The subjects were followed up for at least 6 months after the surgery. The characteristics of the 5 studies are summarized in Table 1.

**RESULTS**

The data of the 5 case-controlled studies were pooled and analyzed based on a fixed-effect model as shown in the Forest plot (Figure 1). Analysis was based on a total sample size of 804 eyes with the weight of each study on the overall effect as follows: Wagner et al. 55.51%, Kato et al. 21.28%, Flesner et al. 3.29%, Krepler et al. 7.07%, and Squirrell et al. 12.84%. Tests for heterogeneity (chi-square)

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**Table 1. Description of nonrandomized, prospective studies.**

<table>
<thead>
<tr>
<th>Study</th>
<th>Population Description</th>
<th>Intervention Description</th>
<th>Comparison</th>
<th>Outcome Measure</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krepler, et al.</td>
<td>42 diabetic patients for unilateral cataract surgery</td>
<td>Phacoemulsification and in-the-bag implantation of an intraocular lens (IOL)</td>
<td>Unoperated fellow eye</td>
<td>Progression of diabetic retinopathy (EDTRS classification)</td>
<td>Prospective, case control</td>
</tr>
<tr>
<td>Squirrell, et al.</td>
<td>50 diabetic patients for unilateral cataract surgery</td>
<td>Phacoemulsification and in-the-bag implantation of an intraocular lens (IOL)</td>
<td>Unoperated fellow eye</td>
<td>Progression of diabetic retinopathy (EDTRS classification)</td>
<td>Prospective, case control</td>
</tr>
<tr>
<td>Flesner, et al.</td>
<td>39 diabetic patients for unilateral cataract surgery</td>
<td>Phacoemulsification and in-the-bag implantation of an intraocular lens (IOL)</td>
<td>Unoperated fellow eye</td>
<td>Progression of diabetic retinopathy (EURODIAB IDDM complications study grading system)</td>
<td>Prospective, case control</td>
</tr>
<tr>
<td>Kato, et al.</td>
<td>66 diabetic patients for unilateral cataract surgery</td>
<td>Phacoemulsification and in-the-bag implantation of an intraocular lens (IOL)</td>
<td>Unoperated fellow eye</td>
<td>Progression of diabetic retinopathy (Fukuda Classification)</td>
<td>Prospective, case control</td>
</tr>
<tr>
<td>Wagner, et al.</td>
<td>205 diabetic patients for unilateral cataract surgery</td>
<td>Phacoemulsification and in-the-bag implantation of an intraocular lens (IOL)</td>
<td>Unoperated fellow eye</td>
<td>Progression of diabetic retinopathy (EDTRS classification)</td>
<td>Prospective, case control</td>
</tr>
</tbody>
</table>
showed homogenous results. The overall event rate showed that 81 of the 363 eyes that underwent phacoemulsification and 63 of the 363 control eyes had progression of diabetic retinopathy. The relative risk-point estimate was 1.36, which was not statistically significant (95% confidence interval, 0.95–1.96).

**DISCUSSION**

There is a large body of literature on the progression of diabetic retinopathy after phacoemulsification, but it consists mainly of retrospective studies, cohort studies, or case series. This review found no randomized, controlled trials on the subject. Five nonrandomized, prospective, case-controlled studies of similar study design were found dealing with the topic. The results of the 5 studies show that uncomplicated phacoemulsification and in-the-bag placement of an intraocular lens (IOL) did not result in increased progression and is, therefore, not contraindicated in patients with diabetic retinopathy. The observed progression after the surgical invasion is postulated to be a part of the natural course of the disease and not a result of the surgery. In all studies, improvement in visual acuity and the ability to better visualize the fundus to monitor and treat the retinopathy outweighed the risks of the surgical procedure and the possibility of later progression.

There is growing evidence to support a more interventional approach to the management of cataract in patients with diabetes mellitus. This refinement in the approach to the timing of cataract surgery in diabetic patients seems to be the most important development in this field. However, it must be emphasized that the studies cited in this review are subject to methodological variation. The definition of retinopathy and determining its severity may vary due to inherent difficulties in grading retinopathy in eyes with cataract. The surgical techniques employed may vary among centers, likewise the indications for laser therapy. Grading the progression of retinopathy and follow-up monitoring can be different among the studies. Thus, the need is apparent for a well-designed, randomized, controlled clinical trial that will assess the progression of diabetic retinopathy after phacoemulsification.

**Implications on practice**

There are no randomized controlled trials to strongly support conclusions regarding the progression of diabetic retinopathy after phacoemulsification. The available studies reviewed have methodological flaws inherent in a nonrandomized or uncontrolled study design. Nonetheless, it seems that modern, uncomplicated, small-incision cataract surgery has minimal influence on the progression of diabetic retinopathy. Meticulous follow-ups are still needed for early detection and treatment of the retinopathy should it progress as a natural course of the disease in order to preserve the visual improvement gained from the cataract surgery.

**Implications on research**

Prospective randomized controlled trials should be conducted in eyes with nonproliferative and proliferative diabetic retinopathy undergoing unilateral phacoemulsification to determine the risk factors for progression of the retinopathy. A well-designed study with adequate sample size, blinded outcome assessment, and long-term follow-up will surely provide statistically significant results to show whether phacoemulsification and any attendant complications are risk factors for progression of diabetic retinopathy.

![Figure 1](https://example.com/figure1.png)

**Figure 1.** Phacoemulsification v. no surgery in the progression of diabetic retinopathy.

<table>
<thead>
<tr>
<th>Study or subcategory</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>OR (fixed) 95% CI</th>
<th>Weight %</th>
<th>OR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wagner, et al.</td>
<td>3/205</td>
<td>35/205</td>
<td></td>
<td>55.51</td>
<td>1.29 (0.79, 2.12)</td>
</tr>
<tr>
<td>Kato, et al.</td>
<td>6/66</td>
<td>14/66</td>
<td></td>
<td>21.28</td>
<td>1.19 (0.53, 2.69)</td>
</tr>
<tr>
<td>Fleshner, et al.</td>
<td>7/39</td>
<td>2/39</td>
<td></td>
<td>3.29</td>
<td>4.05 (0.78, 20.89)</td>
</tr>
<tr>
<td>Krepler, et al.</td>
<td>5/42</td>
<td>4/42</td>
<td></td>
<td>7.07</td>
<td>1.28 (0.32, 5.16)</td>
</tr>
<tr>
<td>Squirrell, et al.</td>
<td>10/50</td>
<td>8/50</td>
<td></td>
<td>12.84</td>
<td>1.31 (0.47, 3.66)</td>
</tr>
<tr>
<td><strong>Total (95%CI)</strong></td>
<td><strong>402</strong></td>
<td><strong>402</strong></td>
<td><strong>100.00 1.36 (0.95, 1.96)</strong></td>
<td><strong>100.00 1.36 (0.95, 1.96)</strong></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Chi² = 1.86, df = 4 (p = 0.76), I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Test for overall effect: Z = 1.66 (p = 0.10)</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**OR** – odds ratio
**CI** – confidence interval

<table>
<thead>
<tr>
<th>OR</th>
<th>0.1</th>
<th>0.2</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>5</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>CI</td>
<td>Favors phacoemulsification</td>
<td>Favors no surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
References