Influence of Intraoperative Course on Visual Outcome after an RPE–Choroid Translocation

Kristel Maaijwee,1 Tom Missotten,2 Paul Mulder,5 and Jan C. van Meurs1,4

PURPOSE. In a previous study, preoperative variables were correlated with postoperative visual outcome after the translocation of a free RPE–choroid graft. The present study was conducted to investigate whether the intraoperative course was an independent factor influencing visual outcome in these patients.

METHODS. This was a prospective interventional case series of 48 patients with exudative AMD treated with an RPE–choroid translocation. Preoperative and postoperative evaluation included ETDRS visual acuity (VA) and fixation testing by a masked examiner. Four critical surgical steps were evaluated, and the intraoperative course was graded from 0 (uncomplicated surgery) to 5 (most complicated surgery). The relationship between intraoperative course adjusted for preoperative delay/lesion composition and visual outcome at 3 months and 1 year after surgery was analyzed with multivariate analysis.

RESULTS. The mean VA (logMAR) improved slightly from 0.99 before surgery to 1.00, 0.94, 0.89, and 0.91 after 3, 6, 9, and 12 months, respectively. Foveal fixation on the graft was present in 34 (71%) of the eyes at 1 year after surgery. The intraoperative course was statistically significantly associated with the ΔVA (logMAR) at 3 months (P = 0.037) and at 1 year after surgery (P = 0.020) and if measured as gain or loss of ≥2 ETDRS-lines (odds ratio [OR] 1.8, 95% confidence interval [CI] 1.7 to 2.8, P = 0.027) and ≥5 ETDRS lines (OR, 2.2, 95% CI 1.9–3.5, P = 0.003); better surgery was associated with visual gain whereas eventful surgery was associated with visual loss.

CONCLUSIONS. The intraoperative course adjusted for preoperative delay/lesion composition and size, percentage of blood, and FAs. Lesion composition (predominantly/minimally classic or occult) was related to visual outcome after surgery.

Therefore, the aim of this study was to investigate whether the intraoperative course might be an independent factor correlating with visual outcome after RPE–choroid translocation for exudative AMD.

PATIENTS AND METHODS

Patients

An RPE–choroid translocation was performed in 48 eyes of 48 consecutive patients with exudative AMD (30 women, 18 men) aged 79 ± 7 (mean ± SD) years (range, 63–96 years) between October 2005 and April 2006 by the same surgeon (JvM). At the time of analysis, all patients had been followed up for at least 1 year after surgery.

Patients were eligible if they had subfoveal choroidal neovascularization (CNV) membrane, with or without submacular blood, not treatable by or not responding to other modalities available at that time in our hospital: laser, PDT (in the Netherlands, this was only available for patients with predominantly classic lesions), or intravitreal bevacizumab (Avastin [Genentech, South San Francisco, CA], available March 2006). Exclusion criteria for surgery included choroidal neovascularization (CNV) with an etiology other than AMD, visual acuity (VA) >20/63, and history of symptomatic visual loss for more than 6 months.

The Institutional Review Board of the Rotterdam Eye Hospital approved the study; informed consent was obtained from all patients in accordance with the ethical standards laid down in the Declaration of Helsinki.

Preoperative examination included best-corrected ETDRS VA (Snellen and logMAR equivalents), dilated funduscopy, and fluorescein angiography (FA). Postoperative visits were scheduled at 1, 3, and 6 weeks and at 3, 6, 9, and 12 months. During each visit, an examiner masked to the intraoperative course performed best-corrected ETDRS VA testing and determined foveal fixation on the graft with biomicroscopy.

Grading of Preoperative Images

A reader (TM) masked for all other preoperative, intraoperative, and postoperative variables assessed the preoperative color fundus images and FAs. Lesion composition (predominantly/minimally classic or occult) was classified with FA according to the Macular Photocoagulation Study (MPS).5 If a lesion was covered with an extensive hemorrhage (≥50% of the lesion), it was labeled a hemorrhagic lesion.

Surgery

After the induction of a posterior vitreous detachment, complete vitrectomy was performed. The CNV was removed from the subretinal

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space with a Thomas subretinal forceps through a paramacular retinotomy in the temporal raphe (Fig. 1A). After circular heavy diathermia in the midperiphery at the 12 o’clock position and removal of the retina within the diathermia marks, vitreous scissors were used to cut a full-thickness graft of RPE–choroid of approximately 2/1100 mm (Fig. 1B). The graft was grasped from the choroidal site with forceps (Fig. 1C) and repositioned under the macula through the existing paramacular retinotomy (Fig. 1D). Perfluorocarbon liquid was injected to keep the graft in place and to facilitate the release of the graft when retracting the instrument. The midperipheral donor site was surrounded with laser coagulation, followed by a silicone oil tamponade. In a second procedure approximately 3 months later, the silicone oil was removed. In patients with phakic lenses, lensectomy was performed during the first surgery, and the intraocular lens (IOL) was inserted during the second surgery.

Grading of Intraoperative Course

Immediately after surgery, the surgeon graded the intraoperative course. Variables included in the grading process were removal of the entire CNV membrane in one extraction, without the need for further manipulation to extract the remaining fibrovascular tissue (yes, 0; no, 1); subretinal insertion of the RPE–choroid graft in one attempt (yes, 0; no, 1); submacular manipulation with a cannula to reposition or flatten the RPE–choroid graft (no, 0; one focused manipulation, 1; more than one manipulation needed, 2); and intraoperative submacular choroidal bleeding (no, 0; yes, 1).

These four variables were scored and added, resulting in an intraoperative course grade from 0 (ideal procedure) to 5 (complicated surgery).

Statistical Analysis

Ordinary multiple linear regression analysis and multiple ordinal logistic regression analysis were used to analyze the relation between intraoperative courses (grades 0–5, nominal values) adjusted for preoperative delay (i.e., time between onset of symptoms and surgery in weeks) and lesion composition (minimally classic, predominantly classic, occult, or hemorrhagic). Outcome variables were ΔVA (logMAR) at 3 months after surgery; ΔVA (logMAR) at 1 year after surgery; and ordinal categorical outcome variables “change of ≥2 or ≥3 ETDRS lines” defined as −1 (≥2 or ≥3 lines loss), 0 (<2 or ≥3 lines loss or gain [i.e., no change]), and 1 (≥2 or ≥3 lines gain) at 1 year after surgery.

To evaluate whether submacular manipulation during surgery could have influenced macular function while it excluded other postoperative complications related to the surgery that influenced the macula, patients with postoperative retinal detachment (RD) over the macula were excluded in a second analysis. All analyses were performed using SPSS (Windows version 12.0; SPSS Inc., Chicago, IL).
patient had a maximal possible score of 5 (Table 1). Surgery was uneventful (score 0) in only six patients. No intraoperative course

48 patients had a preoperative VA after 3, 6, 9, and 12 months, respectively (Fig. 3). Four of the 48 patients had a preoperative VA ≥20/80, and eight had a VA ≥20/80 or better at 1 year after surgery. Foveal fixation on the graft was present in 71% (34 of 48) of the eyes up to the last examination.

According to the MPS criteria, two patients had predominantly classic CNV, seven had minimally classic CNV, 10 had occult CNV, and 29 had hemorrhagic lesion (>50% blood).

Intraoperative Course

Surgery was uneventful (score 0) in only six patients. No patient had a maximal possible score of 5 (Table 1). Complications encountered during surgery (but not used for grading of the intraoperative course) consisted of a CNV membrane attached to the retina (n = 1), RPE damage on the graft (n = 4), entry site retinal tear (n = 1), macula schisis caused by fluid injection (n = 1), choroidal detachment (n = 1), local RD at the entry site tear (n = 1), and inadequate position or flattening of the graft (n = 3).

Complications after Surgery

In 48 eyes, silicone oil was removed 4.6 ± 2.4 months after surgery. At the time of silicone oil removal in all but three patients, the inner limiting membrane was removed over the macula; four of these patients had a biomicroscopically manifest macular pucker.

RD resulting from proliferative vitreoretinopathy (PVR) and involving the macula developed in four patients before and in another six patients after silicone oil removal. Vision dropped to counting fingers in all these patients. Membrane peeling and a silicone oil (seven patients) or gas tamponade (three patients) were performed. In five patients, PVR-RD recurred after retvitrectomy. Revitrectomy was repeated and completed with silicone oil (four patients) or gas tamponade (one patient). The silicone oil was still in five of the eyes at time of analysis. Rhegmatogenous RD originating from the retinotomy site developed in one patient after silicone oil removal. Vision remained stable after revitrectomy with a gas tamponade.

Four subretinal hemorrhages over or beside the graft and one vitreous hemorrhage occurred within 1 day after surgery, 2 after the RPE-choroid translocation, and 3 after silicone oil removal; all were considered related to the surgery.

CNV recurrence or persistence was detected angiographically in 8% (4 of 48) of the eyes from 3 to 12 months after surgery. Two patients were treated with bevacizumab, but in two patients no treatment had been initiated at the time of analysis.

Statistical Analysis

Ordinary multiple linear regression and multiple ordinal logistic regression analyses revealed a statistically significant effect of intraoperative course on all the outcome variables adjusted for preoperative delay and lesion composition: ΔVA (logMAR) at 3 months after surgery (r² = 0.201; P = 0.057) and at 1 year after surgery (r² = 0.259; P = 0.028), change of ≥2 ETDRS lines (OR, 1.8; 95% CI, 1.7–2.8; P = 0.027), and change of ≥3 ETDRS-lines (OR, 2.2; 95% CI, 1.9–3.5; P = 0.003). The effect showed that an increased number of intraoperative complications resulted in a lower postoperative visual outcome.

Some of the four lesion composition groups had low frequencies. Therefore, all analyses were repeated with the lesion

<table>
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<tr>
<th>CNV Removal in One Piece</th>
<th>Insertion of Graft in One Move</th>
<th>Submacular Manipulation of Graft</th>
<th>Submacular Choroidal Bleeding</th>
<th>Total Score</th>
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FIGURE 3. Preoperative VA versus VA at 1 year after surgery (logMAR). Patient group (n = 48) divided according to grading of intraoperative course (score 0–4). Data points above the diagonal line indicate patients with visual improvement.
groups minimally classic, predominantly classic, and occult combined \((n = 19)\), and results were compared with those of the hemorrhagic lesion group \((n = 29)\). However, the results were the same as in the four separate lesion composition groups.

In the second analysis, the 10 patients with RD caused by PVR and involving the macula were excluded. The intraoperative course remained statistically significantly related to \(\Delta VA\) at 3 months after surgery \((\chi^2 = 0.317; P = 0.014)\) and to a change of \(\geq 3\) ETDRS lines \((OR, 1.9; 95\% CI, 1.8–3.1; P = 0.016)\) 1 year after surgery. The relation was not (though it was almost) significant with the outcome variable \(\Delta VA (\chi^2 = 0.252; P = 0.052)\) and a change of \(\geq 2\) ETDRS lines \((OR, 1.6; 95\% CI, 1.5–2.6; P = 0.083)\) 1 year after surgery.

There was no relation between lesion composition (minimally or predominantly classic, occult, or hemorrhagic) and intraoperative course \((P = 0.98; Kruskal-Wallis test)\).

**Discussion**

This study showed a statistically significant relation between the intraoperative course of and the postoperative visual outcome after RPE–choroid translocation in patients with exudative AMD, suggesting that an improved surgical technique may help to improve the visual outcome.\(^6\) This assumption is further supported by the poor long-term visual results in the first series of patients with a free RPE–choroid graft, in whom the graft was harvested from the juxtafoveal site.\(^2\) This technique involved repeated manipulation to the macular area. Moreover, the adjacent RPE and choroid might have been affected by the often longstanding macular degeneration. Taking the graft from the midperiphery, however, decreased submacular surgical manipulations and their associated trauma, which may explain the sustained visual gain in several patients who underwent surgery with the latter technique.\(^3\)\(^4\)\(^6\)

In addition to direct tissue damage, manipulation of the graft or subfoveal site causes dispersion and proliferation of RPE cells, which may increase the risk for PVR formation.\(^8\)\(^9\)

Intraoperative variable submacular choroidal bleeding was taken into account because such bleeding may increase intraoperative manipulations and shearing forces when clot removal is attempted, whereas the remaining blood may damage the retina by iron toxicity or by creating a diffusion barrier and may have a possible negative effect on graft revascularization.\(^10\)

Given the high rate of PVR, it was unclear whether the relation between intraoperative course and postoperative visual outcome resulted from better macular function in patients with better intraoperative courses or by the greater number of postoperative complications in patients with worse intraoperative courses. Therefore, all analyses were repeated, excluding data on patients with RD involving the macula caused by PVR. However, there was still a statistically significant relation between intraoperative course and postoperative visual outcome. These data support the hypothesis of MacLaren et al.\(^7\) that late apoptosis of the photoreceptors and subsequent RPE graft failure may be a result not only of the disease process itself but of the trauma initiated by the surgery.

The relation between intraoperative course and visual outcome was adjusted for preoperative variables as duration of visual loss and type of lesion composition. A previous study showed that lesion composition (predominantly classic and occult lesions did better than hemorrhagic and minimally classic ones) but not duration had a statistically significant influence on visual outcome after 1 year.\(^7\) The present study confirmed that the intraoperative course probably acted as a confounding factor.

The CNV recurrence rate of 8% reported in this study might have been underestimated because fluorescein angiography was performed only if recurrent neovascularization was clinically suspected.

This study showed that the intraoperative course statistically significantly influenced postoperative visual outcome after RPE–choroid translocation. This prompts us to optimize the surgical technique and instrumentation delivered by our multidisciplinary team. Surgery should be a last resort for patients whose conditions are no longer treatable or who are not responding to approaches that entail fewer potential complications, such as anti-VEGF or PDT.

With an optimized technique, RPE–choroid translocation may in the future be combined with local pharmaceutical therapeutics or gene or precursor cell transfer techniques.\(^11\)\(^12\)

**References**


