Risk Factors for Early Filtration Failure Requiring Suture Release After Primary Glaucoma Triple Procedure With Adjunctive Mitomycin

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Purpose: Postoperative release of scleral flap closure suture is useful in trabeculectomy combined with cataract surgery. We determined risk factors for early filtration failure requiring suture release during the first month after primary glaucoma triple procedure.

Methods: The medical records of 71 consecutive patients with primary open-angle glaucoma who underwent a primary glaucoma triple procedure (primary trabeculectomy, phacoemulsification, and posterior chamber intraocular lens implantation) were reviewed. Suture release had been performed in 24 of the patients for early filtration failure with postoperative intraocular pressure greater than the target value during the first postoperative month. The long-term filtration failure was defined according to 2 criteria based on medical dependency and requirement of additional surgical procedure for intraocular pressure control. Cox proportional hazards multivariate analysis was performed to identify independent risk factors.

Results: African American race (P = .02), more than 2 preoperative glaucoma drugs (P = .02), and intraocular pressure greater than 14 mm Hg during the first postoperative week (P = .006) were identified as significant independent risk factors requiring suture release for filtration failure during the first postoperative month. Their significance was further confirmed by Kaplan-Meier survival analysis with Mantel-Cox log-rank test (P = .03, P = .02, and P = .001, respectively).

Conclusions: African American race, more than 2 preoperative medications, and intraocular pressure greater than 14 mm Hg in the first postoperative week are major independent risk factors for initial filtration failure requiring suture release during the first month after primary glaucoma triple procedure. Presence of the risk factors may warrant a more aggressive antiproliferative regimen and/or earlier suture release.


SUTURE RELEASE is commonly performed for lowering intraocular pressure (IOP) after glaucoma filtration procedures. The sutures used to close the scleral flap during trabeculectomy may be released by many different techniques, from removal of releasable sutures1-8 to argon laser suture lysis,9-14 to increase filtration and thereby decrease IOP after trabeculectomy. Kolker et al7 reported that the use of releasable sutures in trabeculectomy allowed them to achieve a low incidence of shallow to flat anterior chamber postoperatively without compromising long-term filtration success. Johnstone et al4 also demonstrated the usefulness of a releasable tamponade suture in maintaining the anterior chamber depth in the early postoperative period while permitting satisfactory filtration after trabeculectomy. Releasable sutures are also routinely used for patients undergoing combined trabeculectomy and cataract surgery.15-18 In fact, the incorporation of releasable sutures and postoperative suture release, either by their removal or by argon laser suture lysis, as well as selective use of adjunctive mitomycin, justifies the combined-procedure approach rather than consecutive trabeculectomy and cataract surgery even in patients with glaucoma whose IOP is out of control with maximum tolerated medications. However, the risk factors requiring release of scleral flap sutures because of early filtration failure in combined trabeculectomy and cataract surgery have not been investigated. The purpose of this study was to determine those risk factors and the efficacy of suture release in patients with early filtration failure after a combined trabeculectomy and cataract surgery.

The demographic and preoperative data gathered on the patients in this study are...
PATIENTS AND METHODS

The study population consisted of 71 eyes of 71 consecutive patients who had primary open-angle glaucoma for which they were receiving medical therapy and visually significant cataract with best-corrected Snellen visual acuity of 20/50 or worse, and who underwent uncomplicated primary glaucoma triple procedure (PGTP) for improvement of both visual acuity and IOP control. All the study eyes had glaucomatous visual field defects of varying severity with abnormal mean deviation and corrected pattern standard deviation global indexes of the Humphrey 24-2 central visual field test, varying degrees of glaucomatous cupping of the optic disc, and a history of elevated IOP of 22 mm Hg or higher before medical therapy. The PGTP consisted of primary trabeculectomy, phacoemulsification, and posterior chamber intraocular lens implantation. All operations were performed by the same surgeon (D.H.S.) with the same technique after each patient gave informed consent approved by the institutional review board.

Local anesthesia was achieved with modified Van Lint and retrobulbar blocks and was followed by injections of 40 mg each of subconjunctival gentamicin sulfate and sub-Tenon triamcinolone acetonide. A 7-mm (chord length) fornix-based conjunctival flap, including Tenon capsule, was made to expose bare sclera in the superior quadrant. An episcleral traction suture was placed 7 mm posterior to the limbus. Then, a limbus-based triangular half-thickness lamellar-scleral flap was dissected that measured 3 mm at the base and 3 mm to the apex from each corner of the base and extended on either side for later insertion of an intraocular lens. At this point, a small piece of cellulose sponge soaked in a 0.5-mg/mL solution of mitomycin with a hydrated dimension of approximately $2 \times 3 \times 7$ mm$^3$ was placed under the conjunctival flap over the dissected scleral flap. The duration of mitomycin application was 1 minute, irrespective of the severity of the glaucoma, IOP control, and number or kind of medications used. After the cellulose sponge was removed, the conjunctival flap was everted and the space between the flap and the episclera was irrigated with a copious amount of balanced salt solution and inspected to ascertain the absence of any sponge fragment.

A paracentesis and an incision into the anterior chamber of about 3.5 mm, capsulorhexis, hydrodissection, and phacoemulsification followed. The capsular bag was inflated with hyaluronate sodium, and the full-thickness corneoscleral incision was enlarged to about 5 mm. A 5 x 6-mm all-polyethylmethacrylate posterior chamber intraocular lens was inserted into the capsular bag. The corneoscleral incision was closed partially with 2 interrupted 9-0 nylon sutures at the base of the scleral flap, and the intraocular lens was rotated with its long axis along the horizontal meridian. A trabeculectomy opening was made under the scleral flap by means of a Gass punch, followed by a peripheral iridectomy with Vannas scissors. The remaining viscoelastic material was removed with an irrigation-aspiration probe. The triangular scleral flap was closed with 1 apical releasable 9-0 nylon suture as previously described. The scleral flap closure was adjusted to be tight enough to allow full inflation of the anterior chamber but not too tight to prevent ingress of a small amount of fluid when balanced salt solution was injected through the paracentesis track. The conjunctival flap was sutured to the listed in Table 1. The patients were followed up to 48 months, with a mean postoperative follow-up of 39.1 +/- 19.2 months. The 2 groups were similar to each other in demographics and preoperative clinical profiles, including the mean predetermined target IOP (the upper limit), except that group 1 had a significantly greater dependence on medications (P = .04) and a significantly greater number or kind of medications used. After the cellulose sponge was removed, the conjunctival flap was everted and the space between the flap and the episclera was irrigated with a copious amount of balanced salt solution and inspected to ascertain the absence of any sponge fragment.

A paracentesis and an incision into the anterior chamber of about 3.5 mm, capsulorhexis, hydrodissection, and phacoemulsification followed. The capsular bag was inflated with hyaluronate sodium, and the full-thickness corneoscleral incision was enlarged to about 5 mm. A 5 x 6-mm all-polyethylmethacrylate posterior chamber intraocular lens was inserted into the capsular bag. The corneoscleral incision was closed partially with 2 interrupted 9-0 nylon sutures at the base of the scleral flap, and the intraocular lens was rotated with its long axis along the horizontal meridian. A trabeculectomy opening was made under the scleral flap by means of a Gass punch, followed by a peripheral iridectomy with Vannas scissors. The remaining viscoelastic material was removed with an irrigation-aspiration probe. The triangular scleral flap was closed with 1 apical releasable 9-0 nylon suture as previously described. The scleral flap closure was adjusted to be tight enough to allow full inflation of the anterior chamber but not too tight to prevent ingress of a small amount of fluid when balanced salt solution was injected through the paracentesis track. The conjunctival flap was sutured to the

postoperative week, which increased to 31 and 25 mm Hg, respectively, by the fourth postoperative week, to require suture release.

We performed Cox proportional hazards multivariate analysis to determine significant risk factors for early filtration failure requiring suture release. Nine possible risk factors were entered as independent covariates in a backward-stepwise Cox proportional hazards regression analysis (the probability values for entry and removal of a variable were set at .05 and .05, respectively). Six of the 9 covariates, such as age, sex, presence of diabetes, presence of hypertension, vertical cup-disc ratio, and preoperative IOP, were not found to significantly affect the early filtration failure requiring a suture release (P > .05, respectively). However, African American race (P = .02), the use of more than 2 preoperative glaucoma medications (P = .02), and an IOP greater than 14 mm Hg after the first postoperative week were found to be significant independent risk factors for early filtration failure requiring suture release. Model coefficients, SEs, risk ratios, and probability values for each of the significant variables affecting the survival time are included in Table 4. Kaplan-Meier survival analysis with Mantel-Cox log-rank test also verified the statistical significances of these 3 independent risk factors (P = .03, P = .02, and P = .001) (Figure 1, Figure 2, and Figure 3).

The 2 groups were then compared as to overall long-term filtration outcome by Kaplan-Meier survival analy-
The result of conjunctival dog ear-like defect was also sealed with a watertight closure with a running 9-0 nylon suture. Balanced salt solution was injected into the anterior chamber to ascertain conjunctival bleb formation and absence of wound leakage.

Postoperative management in all patients included application of an identical topical medical regimen (a corticosteroid-antibiotic ophthalmic ointment at bedtime and 1% prednisolone acetate, 1 drop every hour while awake), which was tapered over several weeks. Digital or focal compression and postoperative suture release were performed whenever necessary to lower the IOP to a target level based on the preoperative history of progression and the severity of the glaucomatous optic nerve damage as described previously. Target IOP was determined as the upper limit of a stable range of pressures unlikely to cause further optic nerve damage in each patient. Digital and focal pressure was applied to the globe at a site immediately posterior to the scleral flap to avoid causing inadvertent leakage of fluid through the leading edge of the conjunctival flap, especially during the first week after surgery.

The scleral flap suture was released when the digital or focal compression was ineffective or when it had to be continued repeatedly beyond the first week after surgery. Suture release was avoided during the first postoperative week and particularly during the first 48 hours because of the risk of overfiltration and secondary complications that can arise from early suture release, especially after intraoperative mitomycin use. After release of the scleral flap suture, digital or focal compression was applied to the globe only if there was no spontaneous increase of filtration. The postoperative management was carried out by the surgeon (D.H.S.) or by his physician assistants under his direct supervision. Filtration surgery was considered an early failure if the postoperative IOP was higher than the upper limit of the target IOP range, necessitating early suture release during the first postoperative month. The long-term filtration success was evaluated according to 2 criteria based on long-term medical dependency and requirement of any additional surgical procedure, including fluorouracil needing revision of the conjunctival bleb for target IOP control: a lenient criterion (criterion A) of target IOP control with not more than 1 glaucoma medication without any additional surgery and a more stringent criterion (criterion B) of target IOP control with no medication or additional surgery.

Demographic and preoperative data were collected. These data included age, race, sex, vertical cup-disc ratio, presence of diabetes, presence of hypertension, preoperative IOP by Goldmann applanation tonometry, the predetermined target IOP, and the number of preoperative glaucoma medications. Postoperative data including IOP, use of glaucoma medications, best-corrected visual acuity, and any additional procedures performed on the patient were collected up to the 48th month postoperatively. The patients were broken up into 2 groups. Group 1 included the patients who required early suture release to reach target IOP within the first postoperative month and group 2 included the patients who did not require early suture release. Demographic data were compared statistically by means of 2-tailed unpaired t test and χ² test between groups 1 and 2. Cox proportional hazards multivariate analysis was performed to identify risk factors for early filtration failure requiring suture release. Unless otherwise indicated, data are given as mean ± SD.

### Table 1. Preoperative Demographics

<table>
<thead>
<tr>
<th>Measure</th>
<th>Total</th>
<th>Group 1</th>
<th>Group 2</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of eyes</td>
<td>71</td>
<td>24</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Age, mean ± SD, y</td>
<td>72.1 ± 3.6</td>
<td>72.7 ± 10.3</td>
<td>71.8 ± 9.3</td>
<td>.71†</td>
</tr>
<tr>
<td>Race, No. black/white</td>
<td>43:28</td>
<td>19:5</td>
<td>24:23</td>
<td>.04</td>
</tr>
<tr>
<td>Sex, No. F/M</td>
<td>47:24</td>
<td>15:9</td>
<td>32:15</td>
<td>.64</td>
</tr>
<tr>
<td>Vertical cup-disc ratio, mean ± SD</td>
<td>0.80 ± 0.13</td>
<td>0.79 ± 0.14</td>
<td>0.80 ± 0.13</td>
<td>.56†</td>
</tr>
<tr>
<td>Preoperative, No. medications, mean ± SD</td>
<td>2.2 ± 1.1</td>
<td>2.7 ± 1.1</td>
<td>2.0 ± 1.1</td>
<td>.01†</td>
</tr>
<tr>
<td>Preoperative intraocular pressure, mean ± SD, mm Hg</td>
<td>20.2 ± 7.3</td>
<td>20.8 ± 7.1</td>
<td>19.9 ± 7.4</td>
<td>.63†</td>
</tr>
<tr>
<td>Predetermined target intraocular pressure, mean ± SD, mm Hg</td>
<td>17.0 ± 1.9</td>
<td>16.8 ± 1.8</td>
<td>17.1 ± 2.0</td>
<td>.46†</td>
</tr>
<tr>
<td>Presence of diabetes, No.</td>
<td>25</td>
<td>5</td>
<td>20</td>
<td>.07</td>
</tr>
<tr>
<td>Presence of hypertension, No.</td>
<td>29</td>
<td>7</td>
<td>22</td>
<td>.15</td>
</tr>
<tr>
<td>Follow-up, mean ± SD, mo</td>
<td>39.1 ± 19.2</td>
<td>44.8 ± 19.5</td>
<td>36.2 ± 18.6</td>
<td>.29†</td>
</tr>
</tbody>
</table>

*χ² test.
†Two-tailed, unpaired t test.

### Table 2. Postoperative Information on Suture Release in Group 1 Patients

<table>
<thead>
<tr>
<th>Measure</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suture release, No. of eyes</td>
<td>24</td>
</tr>
<tr>
<td>Time to suture release, mean ± SD, d</td>
<td>14.3 ± 6.1</td>
</tr>
<tr>
<td>Time to suture release, range, d</td>
<td>3-29</td>
</tr>
<tr>
<td>Postoperative medications at time of suture release, mean No.</td>
<td>0</td>
</tr>
<tr>
<td>Intraocular pressure before suture release, mean ± SD, mm Hg</td>
<td>23.7 ± 6.6*</td>
</tr>
<tr>
<td>Intraocular pressure after suture release, mean ± SD, mm Hg</td>
<td>13.7 ± 6.5*</td>
</tr>
</tbody>
</table>

*P < .001, 2-tailed paired t test.

out a statistically significant difference between the 2 groups according to a more lenient success criterion (criterion A) (P = .27, Kaplan-Meier survival analysis with Mantel-Cox log rank test) (Figure 4). However, group 1 had a significantly greater dependence on medications as well as a higher mean IOP than group 2 at 12 and 24 months postoperatively. The mean number of medications needed postoperatively in group 1 at 12 months was 1.3 ± 1.2 vs 0.5 ± 0.8 in group 2 (P = .007). At 24 months, the mean number of medications needed in group 1 was 1.6 ± 1.2 vs 0.6 ± 0.1 in group 2 (P = .003). At 12 months, the mean IOP of group 1 was 16.6 ± 4.0...
mm Hg vs 14.1 ± 5.5 mm Hg in group 2 (P = .06). At 24 months, the mean IOP in group 1 was 15.8 ± 5.0 mm Hg vs 12.9 ± 5.0 mm Hg in group 2 (P = .05). Thus, when a more stringent success criterion (criterion B) was used, the long-term filtration success rate of group 1 was significantly lower than that of group 2 (P = .02 by Kaplan-Meier survival analysis with Mantel-Cox log-rank test) (Figure 5).

### Commentary

Suture release after trabeculectomy has been a useful adjunct to filtration surgery. It enables the filtration capacity to be increased postoperatively, decreasing the IOP without another invasive procedure. Thus, releasable sutures allow surgeons to achieve a relatively tight closure of the scleral flap intraoperatively, with the assurance that the filtration capacity can be increased as needed during the early postoperative period. In fact, the incorporation of postoperative suture release (either by releasing the suture or by argon laser suture lysis) in addition to selective use of adjunctive mitomycin justifies the combined-procedure approach rather than consecutive trabeculectomy and cataract surgery even in the patient with medically uncontrollable glaucoma and cataracts. Whereas releasable sutures are routinely incorporated and found to be useful in combined trabeculectomy and cataract surgery, the risk factors for early filtration failure requiring suture release have not been investigated.

In our study, significant risk factors for early filtration failure and the subsequent need for early suture release during the first postoperative month after PGTP were found to be African American race, the use of more than 2 glaucoma medications before surgery, and IOP greater than 14 mm Hg in the first postoperative week (Figures 1-3).

Long-term use of topical antiglaucoma medications has been reported to cause conjunctival and episcleral inflammation and fibrosis. A significant increase in the number of macrophages, lymphocytes, mast cells, and fibroblasts as well as a significant decrease in the number of conjunctival epithelial goblet cells have been observed in patients who use antiglaucoma medications for a long period. It is postulated that this fibroblastic proliferation may play a role in causing contraction of newly forming scars that are seen at incisional sites after filtration surgery. Therefore, there is an increased likelihood that early filtration failure and postoperative IOP exceeding the target IOP will require early suture release in patients taking long-term antiglaucoma medications. Not surprisingly, the use of multiple antiglaucoma medications preoperatively is also a risk factor for long-term filtration failure after PGTP. Conversely, trabeculectomy has been reported to be more successful in patients with glaucoma before the use of any antiglaucoma medications.

African American race was another significant risk factor found in this study. This may be explained by the fact that the overall success rate of filtration surgery is

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### Table 3. Complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Total</th>
<th>Group 1</th>
<th>Group 2</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotony (IOP &lt; 6 mm Hg)</td>
<td>9</td>
<td>2</td>
<td>7</td>
<td>.43</td>
</tr>
<tr>
<td>Subconjunctival hemorrhage</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>.46</td>
</tr>
<tr>
<td>Hemorrhage clot in AC</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>.62</td>
</tr>
<tr>
<td>Choroidal detachment</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>.72</td>
</tr>
</tbody>
</table>

*IOP indicates intraocular pressure; AC, anterior chamber.†χ² test.

### Table 4. Coefficients and Risk Estimates for Cox Proportional Hazards Regression Model Relating Risk Factors for Early Filtration Failure Requiring Suture Release

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Coefficient ± SE</th>
<th>Risk Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black race</td>
<td>1.10 ± 0.55</td>
<td>2.98 (1.01-8.82)</td>
<td>.02</td>
</tr>
<tr>
<td>Preoperative medications &gt; 2</td>
<td>0.99 ± 0.43</td>
<td>2.69 (1.16-6.26)</td>
<td>.02</td>
</tr>
<tr>
<td>IOP &gt; 14 mm Hg, first postoperative wk</td>
<td>1.16 ± 0.43</td>
<td>3.70 (1.39-7.35)</td>
<td>.006</td>
</tr>
</tbody>
</table>

*CI indicates confidence interval; IOP, intraocular pressure.

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**Figure 1.** Kaplan-Meier cumulative survival plots comparing the short-term survival between African Americans (n = 43) and whites (n = 26) (P = .03, Mantel-Cox log rank test).

**Figure 2.** Kaplan-Meier cumulative survival plots comparing the short-term survival between patients with 2 or fewer preoperative medications (n = 44) and those with more than 2 (n = 27) (P = .02, Mantel-Cox log rank test).
decreased in African American patients.\textsuperscript{15,17,21,26-31} The success rate has been reported to be as low as \textasciitilde39\% at 2 years postoperatively.\textsuperscript{28} It is also presumed that there is increased fibrovascular proliferation and more vigorous wound healing in African Americans.\textsuperscript{15,17,21,26-31} This response may again cause contraction of the newly forming scars at the site of filtration surgery, leading to early failure of the filtration bleb and need for suture release.\textsuperscript{24} Thus, it is not surprising that African American race is a risk factor for early filtration failure after PGTP. We had also identified African American race as a significant risk factor for long-term filtration failure after PGTP.\textsuperscript{13,17}

The suture release group tended to have elevated IOP beginning in the first postoperative week, although the elevation of IOP was high enough to require suture release in only a portion of the eyes (5/24 [21\%]). In fact, the mean IOP during the first postoperative week was significantly higher in the suture release group than in the group that did not require suture release, and the elevated IOP during the first postoperative week was also a significant independent risk factor for further increase of IOP exceeding the target IOP to require suture release during the first postoperative month. In the absence of the other risk factors, such as African American race and multiple preoperative drug regimen, the cause of elevated IOP during the early postoperative period was most likely to be too-tight closure of the scleral flap wound despite the surgeon's attempt to achieve a closure that was neither too tight nor too loose. In the presence of African American race or more than 2 preoperative medications, however, even inadvertently loose closure of the scleral flap may eventually result in sufficient increase of IOP Within the first postoperative month to require suture release. Cases in point are the 2 eyes in group 1 with early hypotony during the first postoperative week but with elevation of IOP to exceed the target IOP during the fourth postoperative week.

Another finding from this study is that patients who required early suture release had a success rate that approached that of those who did not require early suture release, according to a relatively lenient criterion of success in which target IOP control with the use of not more than 1 medication was considered to be a success (Figure 3). It is probable that without the suture release in the group 1 patients, the success rate might have been significantly worse with the same criterion of success. On the other hand, the statistically insignificant difference between the 2 groups might represent a type II (\(\beta\)) error; it would have taken a sample size of 205 to attain a statistically significant difference (\(P<.05\)) with power greater than 90\%. In fact, the suture release group had a significantly greater dependence on medications as well as a higher mean IOP than the group without suture release at 12 and 24 months postoperatively. Thus, if the more stringent success criterion of target IOP control with no medication was used, the patients who required early suture release had a significantly lower success rate than those who did not require suture release (Figure 5). Without the suture release, however, the group 1 patients might have had a much worse filtration outcome.

A common finding in these patients with early filtration failure and the need for early suture release is the increased fibrovascular proliferation at the trabeculectomy site. In these patients with early failure, releasing the suture after the scleral flap has already started to scar to the underlying sclera may be only partially effective.
in increasing the capacity of outflow at the trabeculectomy site. It is also possible that the aqueous humor during the first month after combined trabeculectomy and cataract surgery may have decreased effectiveness in promoting the development of a filtering bleb.

Therefore, a more aggressive approach before the onset of filtration failure may be warranted in the presence of the risk factors for early filtration failure. The surgeon may take greater care and make a more diligent effort to avoid a too-tight closure of the scleral flap in general and especially in the eyes of African American patients or in the eyes receiving multiple preoperative medications that undergo combined glaucoma and cataract surgery. In addition, earlier suture release, either by itself or combined with a more vigorous use of antiproliferative agents, may overcome the higher rate of filtration failure in patients with the above risk factors. The potential benefit of earlier suture release, such as during the first postoperative week, however, would have to be weighed against the risk of hypotony and related complications that can be associated with very early suture release, especially after intraoperative use of mitomycin.

A more vigorous antiproliferative regimen may consist of a higher intraoperative mitomycin dosage (either longer applicability or higher concentration), supplemented, if necessary, with postoperative fluorouracil injections, especially in the presence of more than 1 risk factor for early filtration failure.

In summary, our study identified African American race, the use of more than 2 preoperative medications, and IOP in the first postoperative week exceeding 14 mm Hg to be major independent risk factors for initial filtration failure requiring early suture release after PGTP. Presence of these risk factors may warrant a more aggressive antiproliferative regimen and/or earlier suture release.

Accepted for publication March 22, 1999.

This research was supported in part by an unrestricted grant from Research to Prevent Blindness Inc, New York, NY.


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