Prospective Evaluation of the First Mitomycin C Augmented Needle Revision in Patients With Failed Nonpenetrating Deep Sclerectomy

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Purpose: The purpose of this study was to evaluate the first mitomycin C (MMC)-augmented needle revision in patients with failed nonpenetrating deep sclerectomy (NPDS) and factors associated with its success.

Materials and Methods: This prospective, nonrandomized comparative trial included 21 consecutive patients (21 eyes) who underwent their first MMC needling revision of failed NPDS blebs. The success was defined as absolute if the IOP decreased >20% from the preoperative value without antiglaucoma treatment and as qualified if that level was achieved with antiglaucoma medications. Preoperative and postoperative factors were evaluated for an association with postoperative success using Kaplan-Meier analysis.

Results: A significant reduction in mean IOP from preoperative levels was evident at the end of the follow-up. The overall surgical success rate was 57.15%. On the basis of Kaplan-Meier survival analysis, we found that patients whose IOP on the following day of the procedure was <8 mm Hg had a higher success rate than those whose 1-day postoperative IOP was higher. These patients had a percentage of success of 100%, 84.6%, and 76.9% at 1-, 3-, and 6-month postoperative follow-up, respectively.

Conclusion: The IOP level on the first postoperative day could be considered a prognostic indicator of success in needling revision performed in failed NPDS.

Key Words: nonpenetrating deep sclerectomy, needle revision, mitomycin C, glaucoma surgery

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Nonpenetrating deep sclerectomy (NPDS) is an alternative to trabeculectomy for the filtration surgery of glaucoma. NPDS has been shown to be effective in reducing intraocular pressure (IOP)1 and is associated with lower rates of intraoperative and postoperative complications than trabeculectomy.2 Long-term studies have shown success rates of 60% to 80% over a period of 3 to 10 years.3,4

In all glaucoma surgery procedures, the healing response is a major problem that can lead to failure of aqueous outflow in some of the operated eyes. Trabeculectomies and NPDS fail because of a mix of subconjunctival, episcleral, and scleral scarring. To decrease the wound healing process, both antifibrotic agents such as mitomycin C (MMC) or 5-fluorouracil, and the Ologen collagen matrix implant have been proposed.5 The needle revision maneuver is a well-established technique to rescue failing blebs and to reestablish the aqueous flow.6 In this sense, Mardelli et al7 have shown in a retrospective study that MMC needle revision is an effective way to revive trabeculectomies. Koukkouli et al8 also reported in a retrospective study that needle revision with subconjunctival MMC may lower IOP in failing NPDS in the long term.

To the best of our knowledge, the outcome features associated with an initial needling revision combined with MMC injection in failed nonencapsulated blebs after NPDS have not yet been studied prospectively. Therefore, we studied the factors that might be related to the success of an initial MMC needling revision of failed NPDS blebs.

MATERIALS AND METHODS

Patients

In this prospective study, we analyzed 21 consecutive patients who underwent needle revision with MMC during approximately 1 year at the Glaucoma Unit of our hospitals. We studied a homogeneous group of patients: all had been diagnosed with primary open-angle glaucoma; they all underwent NPDS (supplemented with MMC and without an implant); the scleral flap was sutured loosely; and the surgery was performed by the same surgeon (C.G.-O.). The procedure was performed after gonioablation had failed to control the IOP. We performed a needling procedure if, based on the progression and severity of glaucoma, an additional reduction of >20% was considered necessary to control the disease.

In all cases, the causes of failure were subconjunctival and episcleral fibrosis. We did not have any encapsulated blebs to include in the study. All analyses were conducted in failed NPDS blebs with adjutative MMC and without an implant, as this is our technique of choice for open-angle glaucoma. Needling revision was indicated in failed blebs, when the IOP was increasing and after Nd:YAG laser gonioablation had failed to control the IOP. We previously...
checked that there was no iris incarceration on the gonioscopy. Needling revision was performed as a primary procedure or when the medical treatment had not achieved the target IOP.

The study was performed according to the principles of the Declaration of Helsinki. The procedure was explained to the patients and written informed consent was obtained from all of them.

**Surgical Technique**

One of the authors (C.G.-O.) performed all the glaucoma surgeries. Needling was performed under sterile conditions and in the operation theater. Under the operating microscope, 1 drop of generic proparacaine 0.5% and 1 of generic povidone-iodine 5% were administered. A sterile lid speculum was inserted. The surgery was performed under subconjunctival anesthesia (0.2 mL of 2% lidocaine). Approximately 10 mm distal to the bleb, a 30 G needle attached to a tuberculin syringe with 2% lidocaine was inserted through the subconjunctival space into the failed bleb and the scleral flap was reached. The needle was then introduced beneath the scleral flap, breaking its adhesions and raising it. Any entry into the anterior chamber was avoided because after NPDS there is a significant risk of iris prolapse through the entry site. Subconjunctival fibrosis was broken by making a fan pattern with the needle. The needling procedure continued until a patent bleb was obvious or when the eye felt soft on digital palpation. Then, a balanced saline solution was introduced into the anterior chamber through paracentesis to verify the drainage, and 0.15 mL 1% acetylcholine was given intracamerally in all cases to avoid iris incarceration. Next, 0.1 mL of MMC (0.2 mg/mL) was injected 10 mm away from the bleb. All cases received an intracameral injection of 0.1 mL cefuroxime (1 mg) at the end of surgery except those patients allergic to penicillin and cephalosporin. The conjunctival entry point was examined for any aqueous leakage. If present, the area was dried with a sterile cotton-tipped swab and cautery was performed with a handheld cautery unit. One drop of generic povidone-iodine 5% and a broad-spectrum topical antibiotic were applied to the eye after the procedure. We did not combine phacoemulsification with the needling procedure in any case. A combination of tobramycin and dexamethasone 0.1% was administered 6 times a day in a tapering dose.

**Surgical Outcomes**

We established 2 outcomes for our study. The primary outcome was needling success, which was achieved if the IOP, measured at the last visit, had decreased >20% without medication from the preoperative period, and with no further surgical or needling procedures required for IOP control during the follow-up period. Qualified success was considered if the IOP had decreased >20% with medication. Surgical failure was defined as an IOP reduction of <20% of the preoperative IOP level despite the use of topical hypotensive medication, or the need for another surgery, including another needling. IOP ≤5 mm Hg plus corneal folds or/and hypotony maculopathy on 2 consecutive follow-up visits after 3 months was also considered as failure. Eyes with IOP ≤5 mm Hg without neither corneal folds nor hypotony maculopathy were considered a success. Several criteria for surgical success or failure can be found in publications (% drop, or IOP levels in mm Hg) but we have considered it more appropriate to define it as explained above. The secondary outcome was to investigate preoperative or postoperative factors that could be predictive of success.

**Ophthalmologic and Anterior Segment Structure Examinations**

All participants underwent a complete ophthalmologic examination that included: Snellen best-corrected visual acuity (BCVA), pupillary reflexes, slit-lamp biomicroscopy and bleb photography, aplation tonometry, ultrasonographic pachymetry, gonioscopy, and ophthalmoscopy. We also determined relevant clinical data, including: the type of glaucoma, IOP, and number and type of medications. Patients were examined preoperatively and postoperatively at day 1 and 1, 3, and 6 months, or more often if necessary.

**Statistical Analysis**

To analyze the evolution of variables during follow-up, we used the paired Student t test or the Wilcoxon signed-rank test. Continuous variables are expressed as mean ± SD. χ² test with Yates correction or Fisher exact test were used to calculate proportion. All tests were 2 tailed and P-values <0.05 were considered statistically significant. The “time to failure” was analyzed using the Kaplan-Meier method. The effects of different preoperative risk factors were analyzed with the log-rank test. Because survival analysis requires a dichotomous response, success and qualified success were both categorized as success. For patients who had bilateral revisions, only the first eye was included in the statistical analysis. Only the first needling was included in the analysis.

All analyses were performed using the statistical program SPSS 19.0 for Windows (SPSS Inc., Chicago, IL).

**RESULTS**

A total of 21 needling procedures were performed on 21 patients. We only analyzed patients who underwent their first needling revision. The mean time from NPDS to the needling revision was 10.00 ± 2.41 months.

Demographic data of the patients is listed in Table 1. There were 12 men and 9 women (mean age, 68.71 ± 10.99 y old; range, 46 to 85 y old). All patients were white and had been diagnosed with primary open-angle glaucoma. In all cases goniopuncture did not achieve the target IOP.

Preoperative and postoperative clinical data for the patients are shown in Table 2. Preoperative BCVA was 0.81 ± 0.20 and decreased significantly to 0.63 ± 0.29 (Wilcoxon test, P = 0.000) and 0.73 ± 0.13 (Wilcoxon test, P = 0.047) at day 1 and at

**TABLE 1. Demographic Data Summary**

| Age (y) | 68.71 ± 10.99 |
|---------|----------------|
| Men/women | 12/9 |
| Type of glaucoma | POAG |
| Number | 21 (100) |
| Surgical procedure | NPDS+MMC (no implant use) |
| Goniopuncture procedure | 21 (100) |
| Time from NPDS surgery to MMC needle revision (mo) | 10 ± 2.41 |

Data are represented in mean ± SD and n (%). MMC indicates mitomycin C; NPDS, nonpenetrating deep sclerectomy; POAG, primary open-angle glaucoma.
1 month of the postoperative period, respectively. However, the differences in BCVA were not statistically significant at 3 months, 0.84 ± 0.16 (Wilcoxon t test, \( P = 0.329 \)) and at 6 months, 0.82 ± 0.29 (Wilcoxon t test, \( P = 0.220 \)) of postoperative follow-up.

A significant reduction of the mean IOP from preoperative levels was evident at the end of the follow-up (Table 2). The mean preoperative IOP was 17.85 ± 2.35 mm Hg, which lowered significantly to 5.42 ± 3.95 mm Hg (a reduction of 69.63%) on the first postoperative day (Wilcoxon t test, \( P = 0.000 \)). The mean postoperative IOP level at 1 month was 14.23 ± 4.27 mm Hg (a reduction of 20.28%) and reduced to 13.14 ± 3.65 mm Hg (a reduction of 23.19%) at 3 months and to 11.80 ± 2.58 mm Hg (a reduction of 20.28%) at 6 months of the follow-up period compared with the preoperative IOP level (Wilcoxon t test, \( P = 0.002, 0.000, 0.000 \), respectively).

Furthermore, the mean preoperative number of topical antiglaucomatous drugs was 1.85 ± 1.27 and decreased significantly to 0.14 ± 0.35 at 1 month and to 1 ± 0.77 at 3 months of the postoperative period (Wilcoxon t test, \( P = 0.000 \) and 0.030, respectively). However, no significant differences were found between the preoperative and postoperative number of topical hypotensive therapies at 6 months (Wilcoxon t test, \( P = 0.799 \)).

On the basis of our IOP criteria of success, there were 4 patients (19.05%) with complete success, 8 patients (38.10%) with qualified success, and 9 patients (42.85%) who were considered failures at the end of the follow-up (6 mo).

On the basis of the Kaplan-Meier cumulative survival plot, 100% of the blebs survived for 1 month, 66.7% survived 3 months, and 57.15% survived for 6 months (Fig. 1). We analyzed the survival curve for several variables that might affect the survival rate, such as age, preneedling IOP, post-needling IOP, and the time passed between NPDS and needling (Table 3). We only found that patients whose IOP on the following day of the procedure was <8 mm Hg had a higher success rate than those whose 1-day postoperative IOP was higher (\( P = 0.016 \)). Those patients with a 1-day postoperative IOP <8 mm Hg had a percentage of success of 100%, 84.6%, and 76.9% at 1-, 3-, and 6-month postoperative follow-up, respectively (Fig. 2).

No serious intraoperative and postoperative complications were found in our patients. We had 4 minor complications (19.04%). However, transient complications were found in 4 eyes; 2 patients showed self-limiting leaks at the conjunctival incisions (9.5%); 1 patient suffered iris incarceration (4.7%) that was resolved with Nd-YAG, and 1 patient showed self-limiting small hyphema (4.7%).

**TABLE 2. Preoperative and Postoperative Clinical Data Summary**

| N = 21 Eyes | Preoperative Data | Postoperative 1 d Data | Postoperative 1 mo Data | Postoperative 3 mo Data | Postoperative 6 mo Data |
|-------------|------------------|-----------------------|------------------------|------------------------|------------------------|
| BCVA (Snellen Scale) | 0.81 ± 0.2 | 0.63 ± 0.29 | 0.73 ± 0.13 | 0.84 ± 0.16 | 0.82 ± 0.29 |
| IOP (mm Hg) | 17.85 ± 2.35 | 5.42 ± 3.95 | 14.23 ± 4.27 | 13.14 ± 3.65 | 11.80 ± 2.58 |
| No. topical hypotensive therapies | 1.85 ± 1.27 | 0.00 | 0.00 | 0.00 | 0.00 |

All data are represented in mean ± SD.

**DISCUSSION**

This study shows that when a NPDS fails due to episcleral or subconjunctival fibrosis, needle revision performed in the operation room and augmented with the subconjunctival injection of MMC can be proposed to maintain function and to preserve the adjacent conjunctiva naive for future surgeries. At 6 months, it achieves a 33.89% drop in IOP.

Our overall success rate of 57.15% at 6 months is lower than the previously published success rates for needle revision after failing NPDS,9 and it is lower than the one we had previously reported for needling after failed trabeculectomies.10 However, it is difficult to compare studies because of the differences in follow-up, surgical techniques, and success criteria. Plausible explanations for these numbers are the following: first, trabeculectomy is a filtering surgery that is less guarded than NPDS, and second, during the needling procedures on trabeculectomies, some surgeons introduce the needle into the anterior chamber (this maneuver is avoided when the needle is performed on NPDS). Both factors may facilitate the entry of a small amount of MMC into the anterior chamber in trabeculectomies. This way, MMC may additionally decrease the production of aqueous humor.

![Survival Functions](image-url)
because of its toxic effect on the ciliary body and therefore decrease the IOP.11,12

Koukkoulli et al10 reported, in a retrospective study, complete and partial success rates of 64% and 71% at 1 year after needle revision of failing NPDS. However, their technique might have been more aggressive than ours, because in some cases they performed 2 or more (range, 1 to 4) needlings (47% of the patients), and we have studied patients in some cases they performed 2 or more (range, 1 to 4) needlings. However, their technique might have been more aggressive than ours, because in some cases they performed 2 or more (range, 1 to 4) needlings (47% of the patients), and we have studied patients who only underwent their first needling. In addition, in some cases they used a 21 G and even a 1.5-mm dual bevel angled paracentesis knife that probably created more extensive disruption of the fibrous tissue but might have caused more complications. We performed the needling with a smaller gauge needle (30 G) and we had less severe complications, and at a smaller rate, than them.

In addition, some factors have been associated with needling success, including age, preneedling IOP, immediate postneedling IOP, and the interval between the initial surgery and the needling.9,10,13–15 We found that a low 1-day IOP (<8 mm Hg) was associated with a higher probability of success. A similar finding was also reported by Shin et al.13 Broadway et al,15 and Than et al16 after needle revision of trabeculectomies. If the physician is able to achieve a very low IOP the day after the procedure, that can be considered at least a preliminary success. This low IOP indicates that the surgeon was able to reestablish a large enough fistula to restore significant flow to the subconjunctival space, and the fistula is more likely to stay patent in the future.13 Therefore, based on our results, it appears that the IOP on the first postoperative day could be considered a prognostic indicator in needling performed in failed NPDS.

Our study had limitations. It was an observational study, it had a small sample size and the follow-up time was short. In contrast, it was prospective, there was uniformity of the needling technique, and we applied a strict success criterion. However, further prospective studies with a higher sample and a longer follow-up are clearly needed to confirm these findings.

In our opinion, needling has a number of advantages compared with redoing or repeating the surgery. It is safe, easy to learn, can be repeated, can be performed at the site originally chosen for filtration (mostly performed under the upper eyelid protection), and does not preclude restoring to other methods for IOP control should it fail, because it preserves the healthy conjunctiva. Therefore, it may be considered before performing a more aggressive surgical intervention when NPDS fails.

In conclusion, at 6 months the procedure achieved a 33.89% drop in IOP, had an overall success rate of 57.15%, and did not change the BCVA. Achieving a low IOP the day after the procedure may be a prognostic success indicator.

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**TABLE 3. Success Rate Analysis of Potential Related Factors**

| Factors                        | N   | P*       |
|--------------------------------|-----|----------|
| Time from NPDS (mo)            |     | 0.394    |
| ≤12                           | 14  |          |
| >12                           | 7   |          |
| Patient age                    |     | 0.134    |
| ≤65                           | 18  |          |
| >65                           | 3   |          |
| Sex                           |     | 0.438    |
| Male                          | 12  |          |
| Female                        | 9   |          |
| Preneedling IOP                |     | 0.313    |
| ≥21                           | 3   |          |
| <21                           | 18  |          |
| Postneedling IOP               |     | 0.016    |
| ≤8                            | 13  |          |
| >8                            | 8   |          |

*Log-rank P-value.
IOP indicates intraocular pressure; NPDS, nonpenetrating deep sclerectomy.

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**FIGURE 2. Kaplan-Meier survival curves of mitomycin C needling revision when 1-day postoperative intraocular pressure (IOP) was <8 mm Hg (upper line) and when IOP was ≥8 mm Hg (lower line).**
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