Randomized Trial on Silicone Intubation in Endoscopic Mechanical Dacryocystorhinostomy (SEND) for Primary Nasolacrimal Duct Obstruction

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Purpose: To study the effect of bicanalicular silicone intubation on endonasal endoscopic mechanical dacryocystorhinostomy (EEM-DCR) for primary acquired nasolacrimal duct obstruction (PANDO).

Design: Randomized clinical trial.

Participants: A total of 120 consecutive adults (103 females) with a presenting age of 64±13.7 years (range, 39–92 years) underwent EEM-DCR for PANDO from November 2005 to May 2009 in a lacrimal referral center.

Methods: The EEM-DCR was performed by 2 lacrimal surgeons using standard techniques. Patients were randomly assigned to receive or not receive bicanalicular silicone intubation for 8 weeks. No antimetabolite was used. All patients received a course of oral antibiotics during nonabsorbable nasal packing for flaps tamponade, which was removed at the first postoperative visit. Patients were assessed at 1, 3, 6, 12, 26, and 52 weeks after the operation.

Main Outcome Measures: Surgical success was defined by symptomatic relief of epiphora, reestablishment of nasolacrimal drainage confirmed by irrigation by 1 masked observer, and positive functional endoscopic dye test by the operative surgeon at 12 months postoperatively. Intraoperative and postoperative complications were recorded.

Results: A total of 118 of the 120 randomized cases completed 12 months of follow-up. Two patients died of unrelated medical illnesses during follow-up. At 12 months postoperatively, there was no statistical difference in the success rate between patients with (96.3%) and without (95.3%) intubation (P=0.79). The odds ratio of failure without silicone intubation was 1.28 (95% confidence interval, 0.21–7.95). There was no difference in the incidence (P=0.97) or the time to develop (P=0.12) granulation tissue between the 2 groups. No significant difference was found between successful and failed cases in terms of age (P=0.21), sex (P=0.37), laterality (P=0.46), mode of anesthesia (P=0.14), surgeon (P=0.26), use of stent (P=0.79), or presence of granulation tissue postoperatively (P=0.39).

Conclusions: The current study design provided 90% statistical power to detect more than 21% difference in surgical outcome, and no such difference was found whether intubation was used or not used in EEM-DCR for PANDO at the 12-month follow-up.

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Methods

Consecutive patients with PANDO who were referred to the lacrimal clinic at the university hospital were recruited. The study was conducted according to the Declaration of Helsinki, with approval obtained from the clinical research ethics committee. Informed consent for operation and randomization were obtained from participants. Both eyes of any eligible patient were allowed to be recruited. Slit-lamp examination of tear film, eyelids, puncta, and anterior segments was performed to rule out reflex tearing, lid laxity, and punctal stenosis. The presence and level of lacrimal obstruction were assessed by lacrimal irrigation and probing. Nasal endoscopy was performed to rule out significant nasal pathology.

Inclusion criteria were (1) adult (aged >18 years) with PANDO confirmed intraoperatively after lacrimal sac exposure and (2) informed consent for the study and randomization.

Exclusion criteria were (1) canalicular obstruction requiring membranectomy intraoperatively; (2) suspected lacrimal sac malignancy; (3) presence of lower lid or punctal ectropion, significant horizontal laxity, or facial nerve palsy; (4) previous lacrimal operation; and (5) previous irradiation, trauma, or major diseases affecting the respective side of nose and orbit.

Standard EEM-DCR with opposing mucosal flaps was performed by 2 attending surgeons. Surgery was performed under general or local anesthesia, according to the patient’s preference. Osteotomy was set superiorly at least 2 mm above the common internal punctum down to the sac-duct junction inferiorly (Fig 1).

Figure 1. Osteotomy was set superiorly at least 2 mm above the common internal punctum down to the sac-duct junction inferiorly in an opened sac with fluorescein flushing through.

Anterior-superiorly, the orbicularis muscle was often exposed (Fig 2), and the agger nasi cells or the operculum of the middle turbinate was frequently entered posterosuperiorly for exposure of the middle turbinate.

Figure 2. Left-sided orbicularis muscle anterior to the unopened lacrimal sac, middle turbinate medially, sac fundus above, and sac-duct junction below (endoscopic intraoperative view). Yellow solid line = lacrimal sac (medial aspect); green dashed line = orbicularis muscle (medial aspect).

Figure 3. Left-sided, unopened agger nasi cell (*) and the operculum of the middle turbinate being partially removed during endonasal endoscopic mechanical dacryocystorhinostomy (EEM-DCR) (endoscopic intraoperative view).

Figure 3. Operculum of middle turbinate.

Figure 4. Left-sided, opened, and marsupialized lacrimal sac with anterior and posterior flaps (endoscopic intraoperative view; same patient as in Fig 2). Yellow solid line = opened lacrimal sac (medial aspect); yellow dashed line = opened lacrimal sac (lateral aspect).
the lacrimal sac fundus\textsuperscript{13} (Fig 3). The lacrimal sac was then incised and marsupialized with anterior and posterior flaps (Fig 4). No antimetabolite was used. Five patients received concomitant endoscopic posterior bony septoplasties (Fig 5A and B) before EEM-DCR by the lacrimal surgeons to improve middle meatal access.

Randomization was carried out by a research assistant who was not involved in the clinical work of this study. Randomization took place after the lacrimal sac was opened intraoperatively to confirm the absence of canalicular obstruction or lacrimal sac pathology. No bilateral simultaneous operation was performed, and each eye was randomized separately for patients with bilateral PANDO. A set of computer-generated random numbers were obtained before randomization and kept in a safety lock. Surgeons and patients had no access to the random numbers throughout the study period. The random numbers were generated in blocks of 10, with equal distribution between either group. Each case was randomly assigned to receive or not receive bicanalicular silicone intubation for 8 weeks.

Previous review at our lacrimal clinic on EEM-DCR revealed that the success rate at 12 months postoperatively was approximately 95\% with silicone stent and 75\% without silicone stent (Chong KKL, unpublished data, July, 2005). By using a 1:1 ratio of control to treatment eyes, a sample size of 65 eyes per group will give a statistical power of 90\% with a type 1 error of 0.05 by chi-square test to detect a difference of 20\% in outcome. A total of 130 eyes were thus recruited to this study.

All patients received a course of oral antibiotics (ampicillin/sulbactam [Unasyn; Pfizer Inc., New York, NY] 375 mg twice daily) and nonabsorbable nasal packing for flaps tamponade, which was removed at the first postoperative visit. Patients were assessed at 1, 3, 6, 12, 26, and 52±2 weeks postoperatively.

Surgical success\textsuperscript{14,15} was defined as (1) symptomatic relief of preoperative epiphora or mucocele, (2) patency of tear drainage as confirmed by lacrimal irrigation performed by 1 masked observer (an ophthalmology resident), and (3) spontaneous fluorescein stain flow into the rhinostomy after application to the conjunctival cul-de-sac (functional endoscopic dye test [FEDT])\textsuperscript{16} by one of the operative surgeons at 12 months postoperatively.

Anatomical failure was defined as regurgitation on irrigation and a closed intranasal ostium. Functional failure was defined as return of epiphora and negative FEDT but patent on irrigation and an opened intranasal ostium.

Any intraoperative or postoperative complication was recorded, including the postoperative appearance of granulation tissue in the intranasal ostium. Endoscopic photographs of the intranasal ostia were taken at each visit. Photographs 12 months postoperatively were graded by one of the operating surgeons masked to the group assignment. The ostium size was compared with standardized photographs of a large ostium and a small ostium.

Statistical analysis was performed with commercially available software: Microsoft Office Excel 2007 (Microsoft Corp, Redmond, WA) and SPSS 16 (SPSS Inc., Chicago, IL). Results of the first eye were used for primary analysis. A separate set of data including the 10 second eyes recruited per protocol were analyzed using a linear mixed model (Stata v. 10.0; StataCorp, College Station, TX) to account for potential correlation between eyes from the same individuals. Numeric data were expressed as mean ± standard deviation.

| Table 1. Baseline Characteristics (Second Eye Included, n=128) |
|---|---|---|
| **With Silicone Tube (65 Cases)** | **Without Silicone Tube (65 Cases)** | **P Value** |
| Age, yrs (mean ± SD [range]) | 64.1±13.6 (39–87) | 63.1±13.8 (39–92) | 0.45\textsuperscript{1} |
| Female:male | 57:8 (87.7%:12.3%) | 56:9 (86.2%:13.8%) | 0.80\textsuperscript{1} |
| Right:left | 35:30 (53.8%:46.2%) | 38:27 (58.5%:41.5%) | 0.60\textsuperscript{1} |
| General:local anesthesia | 32:33 (49.2%:50.8%) | 30:35 (46.2%:53.8%) | 0.60\textsuperscript{1} |
| Surgeon A:surgeon B | 23:42 (35.4%:64.6%) | 24:41 (36.9%:63.1%) | 0.86\textsuperscript{1} |
| Osteotomy size (mm) | 18±2 | 16±3 | 0.23\textsuperscript{1} |

SD = standard deviation.
\textsuperscript{1}Two-tailed independent t test.
\textsuperscript{2}Two-tailed chi-square test.
Chi-square tests were used for comparison of categoric variables and proportions. Continuous variables were compared by unpaired t tests. All P values were 2-tailed and considered significant if <0.05.

Results

A total of 171 lacrimal referrals were evaluated. After excluding 51 patients because of canalicular obstruction (n=30), revision lacrimal surgeries (n=18), history of irradiation (n=2), and midfacial trauma (n=1), 120 patients with 130 cases of PANDO (10 bilateral cases) were randomized (Table 1). Two patients (1 female), aged 77 and 80 years, died of unrelated medical illnesses during follow-up. Both patients were in the intubated group with follow-up to 4 and 7 weeks postoperatively. The results of 118 patients (102 female) were available at the 12-month follow-up.

The mean age of patients was 64±13.7 years (range, 39–92 years). A total of 103 patients (85.8%) were female. Sixty-five patients (50%) received no intubation. By using only the first eye from each recruited patient (n=118), the intubated and control groups were comparable in terms of age, sex ratio, side of operation, anesthesia method, surgeons, and osteotomy size (Table 2).

Among the 118 patients (first eye), 113 (95.8%) achieved surgical success at the 12-month follow-up. Among the 5 failed cases, 2 patients had silicone intubation and 3 patients did not. Three patients had closed ostia (anatomic failure) and 2 patients had open ostia and patent on lacrimal irrigation but return of epiphora (functional failure) (Fig 6A, available at http://aaojournal.org). One patient also developed mucosal adhesion of the ostium with middle turbinate (Fig 6A, available at http://aaojournal.org). One patient who refused further intervention, the other 4 patients received revision EEM-DCR with intraoperative mitomycin C application and bicanalicular intubation and achieved anatomic and functional patency at their last follow-up visits.

By using only the first eye (n=118) for analysis, there was no statistical difference in surgical success between patients with (96.3%) and without (95.3%) intubation (P=0.79) at 12 months postoperatively. The odds ratio of failure without silicone intubation was 1.28 (95% CI, 0.21–7.95). With 54 patients in 1 group and 64 patients in the other, the study had 90% statistical power to detect a 21% difference in surgical outcome between the groups, and no such difference was found. No significant difference was found in the mean time to failure (P=0.14), ostial size at 12 months (P=0.16), incidence (P=0.97), or time to development (P=0.12) of granulation tissue between the 2 groups (Table 4).

When second eyes also were included for analysis per protocol (n=128), no statistical difference in surgical success was found between patients with (96.8%) and without (95.3%) intubation (P=0.67, linear mixed model) at 12 months postoperatively. The odds ratio of failure without silicone intubation was 1.48 (95% CI, 0.24–9.14). With 63 patients in the other and 64 patients in 1 group, the study had 90% statistical power to detect a 20% difference in surgical outcome between the groups, and no such difference was found. No significant difference was found in the mean time to failure (P=0.14), ostial size at 12 months (P=0.24), incidence (P=0.70), or time to development (P=0.13) of granulation tissue between the 2 groups (Table 5).

At 12 months postoperatively, there was no significant difference between successful and failed cases in age (P=0.21), sex (P=0.37), laterality (P=0.46), surgeon (P=0.26), use of stent (P=0.79), presence of granulation (P=0.39), or mode of anesthesia (P=0.14) (Table 6).

A history or subsequent development of contralateral PANDO (i.e., bilaterality) was significantly more prevalent among failed cases (3 of the 5 failed cases were patients with bilateral PANDO) than successful cases (17 of 123 successful cases were patients with bilateral PANDO) (P=0.005) (Table 7).

Three patients (2.3%) had intraoperative orbital fat prolapse when the lateral wall of the lacrimal sac was violated. Eight patients (6.3%) had postoperative nasal mucosal adhesion. Seven patients (5.5%) had epistaxis upon the removal of packing material at the first postoperative visit. In the intubated group (n=63), 4 patients (6.3%) had tube prolapse, which was endoscopically reduced in the office in all patients. Three of these 4 patients had a successful outcome at 12 months. One patient had return of epiphora with an open ostium (functional failure). One patient (1.6%) had stent extrusion 4 weeks postoperatively. This patient achieved surgical success at the 12-month follow-up. One patient (1.6%) had lacrimal false passage during probing intraoperatively.
Discussion

Although external DCR has been considered the gold standard in lacrimal operation, the more recently published series of endonasal DCR in both ophthalmic and otolaryngologic literature report higher success rates compared with prior studies.\(^{11,12}\) This likely reflects an increased familiarity with endoscopic instrumentation and anatomy among lacrimal surgeons and an improved understanding and control of nasolacrimal mucosal healing.\(^2\)

Evidence continues to show that the endonasal approach offers distinct advantages over external DCR. Endonasal DCR preserves lacrimal pump function without damaging the deep pretarsal orbicularis muscle (Horner’s muscle) and the peripheral fibers of the zygomatic and buccal branches of the facial nerve.\(^{17}\) It also avoids disinsertion of the medial canthal tendon.\(^{18}\) Full-thickness scarring from skin to nasal mucosa may occur after external DCR, which may form ring contracture and negatively affect lacrimal sac movement during blinking.\(^{19,20}\) Ancillary procedures, such as septoplasty and middle turbinoplasty/turbinectomy, can be performed simultaneously to improve intraoperative access and to minimize postoperative adhesion.

Progressive ostial fibrosis with or without adhesion to the nasal septum or middle turbinate, inadequately sized or inappropriately located bony and soft tissue ostia, and unrecognized or postoperative canalicular obstruction are common causes of failure in DCR.\(^{21}\) On the other hand, mucosal healing inevitably reduces the size of internal ostium after DCR.\(^{22,23}\) Various adjuvant treatments, including antimetabolites\(^{24}\) (i.e., 5-fluorouracil, mitomycin-C, absorbable packing [e.g., Gelfoam {Pharmacia & Upjohn Co., New York, NY} with\(^{25}\) or without topical steroid\(^{11,12}\) or Merogel {Medtronic Xomed, Jacksonville, FL}\(^{26}\)) have been used to maintain the patency of the ostium. Mechanical stents\(^8\) of different materials, with or without expansile properties, have been used to prevent closure of the “soft tissue” ostium around the internal punctum.

The use of transcanalicular stent was first introduced by Graue and Glenie, who placed a silver wire through the lower punctum into the nose.\(^8\) Gibbs\(^{27}\) then described a technique of silicone rubber tubing for intubation in DCR, although Quickert and Dryden\(^{28}\) were often credited for their contribution to this advance. In their reviews of lacrimal surgery, Anderson\(^{29}\) and Patrinely\(^{30}\) stated that silicone canalicular intubation was “probably the most important recent advance in lacrimal surgery” but it was “not necessary for routine DCR.”

The added benefit of silicone intubation in PANDO during EEM-DCR was not demonstrated by previous studies.\(^3\) In a retrospective study, success was achieved in 85.7% of the intubated cases versus 81.3% of nonintubated cases\(^4\) at a mean follow-up of 23 months using symptomatic improvement as the successful criterion. In a recent randomized trial of 46 cases of PANDO using EEM-DCR, surgical success, defined by symptomatic relief and patency to irrigation at 6 months postoperatively, was achieved by 100% for the nonintubated cases versus 78% for the intubated cases.\(^{32}\) Unlu et al\(^4\) suggested that silicone intubation may predispose to granulation formation with subsequent rhinostomy closure. To date, there is a lack of large-scale, randomized trials with a sufficient follow-up outside of the context of EEM-DCR.

### Table 4. Outcome at 12 Months Postoperatively (First Eye Only, n=118)

<table>
<thead>
<tr>
<th></th>
<th>With Silicone Tube (54 Cases)*</th>
<th>Without Silicone Tube (64 Cases)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success at 12 mos (yes/no)</td>
<td>52:2 (96.3%; 3.7%)</td>
<td>61:3 (95.3%; 4.7%)</td>
<td>0.79(^{1})</td>
</tr>
<tr>
<td>Time to failure (mos)</td>
<td>4.0±1.4</td>
<td>7.0±1.7</td>
<td>0.14(^{1})</td>
</tr>
<tr>
<td>Presence of granulation tissue (yes/no)</td>
<td>23:31 (42.6%; 57.4%)</td>
<td>27:37 (42.2%; 57.8%)</td>
<td>0.97(^{1})</td>
</tr>
<tr>
<td>Time to granulation tissue development (wks)</td>
<td>5.9±3.4</td>
<td>4.3±3.8</td>
<td>0.12(^{1})</td>
</tr>
<tr>
<td>Ostial appearance at 12 mos (large:small)</td>
<td>12:42 (22.2%; 77.8%)</td>
<td>8:56 (12.5%; 87.5%)</td>
<td>0.16(^{1})</td>
</tr>
</tbody>
</table>

*Two patients died of unrelated medical illnesses.
\(^{1}\)Two-tailed chi-square test.
\(^{2}\)Two-tailed independent t test.

### Table 5. Outcome at 12 Months Postoperatively (Second Eye Included, n=128)

<table>
<thead>
<tr>
<th></th>
<th>With Silicone Tube (63 Cases)*</th>
<th>Without Silicone Tube (65 Cases)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success at 12 mos (yes/no)</td>
<td>61:2 (96.8%; 3.2%)</td>
<td>62:3 (95.4%; 4.6%)</td>
<td>0.68(^{1})</td>
</tr>
<tr>
<td>Time to failure (mos)</td>
<td>4.0±1.4</td>
<td>7.0±1.7</td>
<td>0.14(^{1})</td>
</tr>
<tr>
<td>Presence of granulation tissue (yes/no)</td>
<td>25:38 (39.7%; 60.3%)</td>
<td>28:37 (43.1%; 56.9%)</td>
<td>0.70(^{1})</td>
</tr>
<tr>
<td>Time to granulation tissue development (wks)</td>
<td>5.4±1.9</td>
<td>6.6±3.1</td>
<td>0.13(^{1})</td>
</tr>
<tr>
<td>Ostial appearance (large:small)</td>
<td>12:51 (19.1%; 80.9%)</td>
<td>8:57 (12.3%; 87.7%)</td>
<td>0.24(^{1})</td>
</tr>
</tbody>
</table>

*Two patients died of unrelated medical illnesses.
\(^{1}\)Linear mixed model.
\(^{2}\)Two-tailed independent t test.
period to study the efficacy of silicone intubation in EEM-DCR for PANDO.10,31

In this study, silicone intubation did not affect the outcome \((P=0.79)\) at 12 months’ follow-up, the incidence \((P=0.97)\), and the time \((P=0.12)\) to develop granulation tissue. Success rates of the intubated and nonintubated groups using strict criteria16 were 96.3% and 95.3%, respectively. The results of our randomized study concur with the existing literature. Surgical success in a nonrandomized series of 38 cases of PANDO was comparable with \((89.5\%)\) and without \((94.7\%)\) intubation after a median follow-up of 8 years.33 Unlu et al,4 Madge and Selva,8 and Saiju et al9 supported that canalicular intubation did not play an important role in the outcome of external or endonasal DCR performed for PANDO. Silicone intubation may lead to stent prolapse or loss, ocular surface irritation, laceration of canalici, and creation of false passage during insertion.3,8,31 Moreover, retained stent material may cause failure. The results of our study do not support routine intubation in EEM-DCR for PANDO. However, because our study was limited to cases of PANDO, the benefit of bicanalicular silicone intubation in other disorders, such as concomitant canalicular obstruction, needs to be further investigated.

In a histologic study comparing lacrimal sac biopsies obtained from primary and secondary DCRs, the authors found no difference in the amount of inflammatory changes in the revision cases with or without previous intubation. Recurrence was explained by severe fibrotic changes at the rhinostomy site, which was suggested to be related to postoperative tissue repair rather than the effect of silicone stent.34 Contrary to our anecdotal belief, the incidence or the time to development of granulation tissue did not differ significantly between patients with and without silicone intubation in this study.

Success rates of nonintubated endoscopic DCR ranged from 74% to 92.3% at 8 to 49 months of follow-up.4–6,27,31 The success rate of nonintubated DCR in our study was 95.3% at 12-month follow-up. This may be attributed to atraumatic creation of a large osteotomy2 with adequate superior bony clearance (at least 2 mm above internal punctum), complete marsupialization of the lacrimal sac,20 maximal preservation of the nasal and sac mucosa, promoting edge-to-edge healing11,12,25 and regular endoscopic monitoring of ostial healing during the early postoperative period. Frequent endoscopic toileting with debridement of “ostial-threatening” granulation tissue (Fig 7A–F; available at http://aaojournal.org) may lead to an improved outcome that is yet to be verified in future prospective trials.

In conclusion, patients with a history or subsequent development of contralateral PANDO (i.e., bilaterality) had a higher chance of failure (3/20) than those with unilateral disease (2 of 108) \((P=0.005)\). Sodhi et al35 suggested young age as a risk factor for failure of lacrimal drainage surgery. In our study, patients with failure tended to be younger, although this was not statistically significant (Table 4). Intraoperative endonasal access, bony clearance, size, mobility, and degree of marsupialization of the sac and immunopathohistologic changes of nasal mucosa have been identified as possible predictors of outcome.20,36 Further prospective trials using these preoperative and intraoperative parameters will help to identify high-risk subgroups for operative adjuncts, for example, stent or antimetabolites in EEM-DCR.

### References


Footnotes and Financial Disclosures

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