

How to Accelerate Very Early Recovery of Small Incision Lenticular Extraction Formyopia

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Research Article

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28 **Abstract**

29 **Significance:** A relatively long period of time is required for visual recovery after
30 small incision lenticule extraction (SMILE), limiting its possible widespread
31 application. The aim of this study was to compare the impact of different defined
32 daily dose systems of 0.1% fluorometholone in the very early phase after SMILE
33 operation.

34 **Methods:** One hundred and eighty patients (360 eyes) treated with SMILE were
35 divided into three groups. Group A: 60 patients (120 eyes were not given any 0.1%
36 FML; Group B: 60 patients (120 eyes, were given 0.1% fluorometholone once every
37 hour); Group C: 60 patients (120 eyes, were given 0.1% fluorometholone every half
38 an hour). Visual acuity, incidence of subject symptoms and optical quality were
39 assessed at 2, 4 and 24 h postoperatively.

40 **Results:** The optical quality in group C was significantly higher than the other two
41 groups ($p < 0.0001$). The incidence of subject symptoms in group C was also notably
42 lower. There were no significant differences between patient groups at 24h.

43 **Conclusions:** In conclusion, corneal healing, visual and optical quality assessment of
44 patients treated with 0.1% fluorometholone (q1/2h) in the first 2h after SMILE were
45 significantly improved in the very early postoperative phase.

46
47 **Keywords:** Myopia, Small incision lenticule extraction, Fluorometholone, Very early
48 phase

57 **Introduction**

58 Small incision lenticule extraction is a new type of procedure for treating refractive
59 errors, especially myopia and myopia astigmatism. It was developed on the basis
60 offemtosecond laser-assisted in situ keratomileusis (LASIK) and is now considered a
61 safer procedure, as it has a reduced risk of postoperative corneal flap complications¹.
62 Small incision lenticule extraction has been reported to have good long term outcomes
63 in terms of safety, efficacy, predictability, and stability^{2,3}. Nonetheless, compared to
64 LASIK, it has a longer visual recovery time^{4,5} which limits its application. Currently
65 very little is known about the influence of different treatment regimens on patient
66 recovery during the very early phase post Small incision lenticule extraction, i.e.
67 within the first two hours.

68 The use of topical 0.1% fluorometholone has shown a faster resolution of
69 post-operative symptoms and reduction of the very early inflammatory and wound
70 healing responses after Small incision lenticule extraction⁶. This study aimed to
71 investigate the impact of 0.1% fluorometholone in different defined daily dose
72 systems of 0.1% fluorometholone in the very early phase (within 2h) after Small
73 incision lenticule extraction. Visual acuity and a series of visual quality-related
74 indexes were evaluated at 2, 4 and 24h postoperatively.

75 **Materials and Methods**

76 *Ethics statement*

77 All interventions approved by the Institutional Review Board of Fujian Medical
78 University (Fuzhou, China), and were conducted according to the principles in the
79 Declaration of Helsinki.

80 *Participants and procedures*

81 In the present study, 180 patients (360 eyes) who underwent Small incision
82 lenticule extraction procedure at our center from July 2019 to November 2019 were
83 recruited. Small incision lenticule extraction was performed using the Visu Max fem
84 to second laser (Zeiss, Oberkochen, Germany). The following femtosecond laser
85 parameters were used: 120 µm cap thickness, 7.5mm diameter of the cap, and 6.5mm
86 diameter of the posterior lenticule surface. A 2 mm long (32°) corneal incision was

87 made at the 11 o'clock position. The remaining tissue bridges were disrupted using a
88 thin, blunt spatula, and the lenticule was removed through the small incision with
89 microforceps.

90 All subjects were divided into three groups depending on different defined daily
91 dose systems of 0.1% fluorometholone administered during the first 2h after Small
92 incision lenticule extraction. Group A: 60 patients (120 eyes, control group) were not
93 given any 0.1% fluorometholone , Group B: 60 patients (120 eyes) were given 0.1%
94 fluorometholone (once every hour, qh); Group C: 60 patients (120 eyes) were given
95 0.1% fluorometholone (every half hour, q 1/2h).

96 ***Measurement of visual indicators***

97 Optical Quality Analysis System II (OQAS, Visiometrics, Terrassa, Spain) was used
98 to collect retinal images derived from an electric light source and analyze their point
99 spread function characteristics using the dual-channel technique⁷. The visual
100 quality-related indexes, including cutoff for modulation transfer function, Strehl ratio
101 and objective scattering index were produced and compared with vision or contrast
102 sensitivity. These measures can reflect better the muddy degree of the refractive media
103 of human eyes and define the source of visual quality problems objectively. SR
104 indicates the ratio of the light intensity of the Gaussian image point between defective
105 and perfect refractive media (0.15 in healthy adults), in which a higher value
106 represents better visual quality. The modulation transfer function cutoff is the value
107 near which the spatial frequency represents the peak resolving capacity in the
108 modulation transfer function curves. The modulation transfer function cutoff is ≥ 30
109 cpd in adults with normal vision; and higher value represents better visual quality.
110 Objective scattering index is < 2 for healthy adults, and higher value represents
111 muddier refractive media and worse visual quality. Modulation transfer function,
112 Strehl ratio and objective scattering index were measured at 24h preoperatively and 2,
113 4 and 24h postoperatively. Visual acuity (logMAR) and incidence of subjective
114 symptoms were also assessed at 2, 4 and 24h postoperatively.

115 Patients were asked for the presence of subjective symptoms, namely foreign body
116 sensation, eye soreness, eye dryness and blurred vision. The incidence among the

117 three groups was recorded at 2, 4 and 24h after Small incision lenticule extraction.

118 ***Statistical analysis***

119 All statistical analyses were performed using SPSS 18.0 (SPSS Inc., Chicago,
120 Illinois, USA). Two-way ANOVA was applied to compare differences in visual
121 acuity, incidence of subjective symptoms, objective scattering index, modulation
122 transfer function cutoff, and Strehl ratio between these three groups. A p value of <
123 0.05 was considered statistically significant.

124 **Results**

125 ***Study subjects***

126 The demographics of the study population are summarized in Table 1. No
127 significant differences were found in terms of corrected distance visual acuity
128 (logMAR), mean spherical equivalent, or intraocular pressure. The age and sex
129 distributions were also comparable between the three groups. Notably there were no
130 intra-operative complications.

131 ***Impact of 0.1% fluorometholone treatment***

132 To further study the impact of different defined daily dose systems of 0.1%
133 fluorometholone, we conducted visual tests for each group of patients (Fig.1). The
134 visual acuity of all patients had recovered to below 0 at 24h after operation, indicating
135 that Small incision lenticule extraction is an effective procedure for myopia treatment.
136 However, notably at 2 and 4h after surgery, the visual acuity of group C was
137 significantly better compared to the other two groups. Number of eyes recovering
138 higher than 1.0 (logMAR 0.0) were significantly higher in group C compared to
139 Group A and B (114 eyes at 2h and 119 eyes at 4h vs 35 eyes at 2h and 86 eyes at 4h vs
140 8 eyes at 2h and 38 eyes at 4h respectively). Significant differences in modulation
141 transfer function cutoff, Strehl ratio and objective scattering index were also seen
142 between different treatment groups at 2 and 4h postoperatively, summarized in Tables
143 2 and 3. Group C had higher modulation transfer function cutoff, Strehl ratio and
144 objective scattering index compared to the rest. No differences were detected in all
145 examined parameters 24h after surgery, summarized in Table 4.

146 We also investigated the incidence of subjective symptoms among the three groups

147 at 2, 4 and 24h after Small incision lenticule extraction. All groups reported a gradual
148 decrease over time. Notably, patients in Group C reported much lower incidence at 2
149 and 4h postoperatively, summarized in Table 5. At 2h, the incidence of subjective
150 symptoms in group C was 38.33% (46 eyes), compared to 66.67% (80 eyes) in group
151 B and 98.33% (118 eyes) in group A. At 4h, the incidence of subjective symptoms in
152 group C was 18.33% (22 eyes) compared to 35% (42 eyes) in group B and 68.33%
153 (82 eyes) in group A. There was no difference between groups after 24h.

154 **Discussion**

155 Small incision lenticule extraction is increasingly becoming a popular procedure for
156 the treatment of myopia and myopia astigmatism. Its main advantage is an improved
157 safety profile that lacks corneal flap complications⁸⁻¹⁰. However, it still requires a
158 longer period of time for corneal wound and visual recovery compared to LASIK^{4,5}.
159 Currently, little is known about possible influence factors and clinical outcomes in the
160 very early stage of recovery.

161 In the past few years, it has been reported that treatment using topical 0.1%
162 fluorometholone resulted in faster improvement of subjective symptom safer corneal
163 surgery¹¹ and could reduce the very early inflammatory and wound healing responses
164 post Small incision lenticule extraction^{12,13} via improving the tear film stability and
165 corneal epithelium damage due to decreased corneal sensation. It is reported that the
166 operation mechanical stimulus and laser effect could induce the inflammatory
167 response including the secretion of inflammatory cytokines and corneal edema in the
168 very early postoperative period delaying the corneal wound healing and optical
169 quality recovery¹⁴. Using 0.1% fluorometholone and increasing its frequency in the
170 very early stage (within 2h postoperatively) could inhibit pro-inflammatory responses
171 and reduce the subsequent corneal edema and opacity.

172 This study aimed to compare the impact of different different defined daily dose
173 systems of 0.1% fluorometholone in the very early phase post Small incision lenticule
174 extraction (within 2h) with a follow-up time of 24h. Currently fluorometholone is not
175 routinely used during the first post-operative day. It is commonly administered four
176 times a day from the second post-operative day onwards⁴ and has shown slow vision

177 recovery^{4,5}. This study provides valuable information for comparing clinical outcomes
178 such as visual acuity, optical quality and the incidence of subject symptoms. To our
179 knowledge, this is the first report focusing on the acceleration of the recovery process
180 in the very early recovery phase.

181 A total of 180 patients (360 eyes) undergoing Small incision lenticule extraction
182 were enrolled in our study. They were divided into three groups depending on the
183 frequency of 0.1% fluorometholone in the first 2h after surgery. Every clinical
184 outcome was measured three times at each time point, and got the average value was
185 calculated. Even though all the patients had satisfactory outcomes at 24h after surgery,
186 the visual acuity (logMAR), incidence of subject symptoms and optical quality were
187 significantly different at 2 and 4h after surgery. In this study, visual acuity was
188 normalized much faster in group C which was given 0.1% fluorometholone (q 1/2h).
189 It should be noted that at 2, 4 h after surgery, the visual acuity of group C was
190 significantly better compared with the other two groups. Number of eyes recovering
191 higher than 1.0 (logMAR 0.0) were also markedly higher in group C compared to two
192 other groups.

193 Significant differences in modulation transfer function cutoff, Strehl ratio and
194 objective scattering index were seen between different patient groups at 2 and 4 h
195 after surgery, which were diminished 24h after surgery. We also investigated the
196 incidence of subjective symptoms among the three groups at 2h, 4 and 24h time points.
197 The incidence of subjective symptoms, including foreign body sensation, eyes oreness,
198 eye dryness and blurred vision, gradually decreased after surgery in all patient groups.
199 However, the incidence inpatient group C was significantly lower than the other two
200 groups at 2 and 4h post-surgery. A reasonable explanation would be that the increased
201 frequency of fluorometholone use reduced patient discomfort because of reduced
202 inflammation. After 24h, there was no significant difference between these three
203 groups. Overall, our data showed improved impact of 0.1% fluorometholone on
204 clinical outcomes and future studies are needed in order to investigate the mechanistic
205 aspect of these events.

206 **Conclusion**

207 This is the first report examining the clinical outcomes after treatment with 0.1%
208 fluorometholone in the very early phase post Small incision lenticule extraction. Our
209 study supports the use of 0.1% fluorometholone and increasing its frequency in the
210 very early stage (within 2h after Small incision lenticule extraction). Treatment
211 regimen of 0.1% fluorometholone every half an hour resulted in acceleration of the
212 recovery process, measured by evaluation of visual acuity, modulation transfer
213 function cutoff, Strehl ratio and objective scattering index and patient subjective
214 symptoms. In addition, corneal wound healing, visual and optical quality outcomes
215 were also improved. Overall, our findings can contribute to improved patient
216 satisfaction after surgery and therefore promote the application of Small incision
217 lenticule extraction procedure.

218 **Value Statement**

219 WHAT WAS KNOWN:

- 220 1. Small incision lenticule extraction (Small incision lenticule extraction) procedure
221 has become a popular technique for treating myopia and myopia astigmatism.
- 222 2. A longer period of time is required for visual recovery from Small incision
223 lenticule extraction operation, limiting its wide spread application.

224 WHAT THIS PAPER ADDS:

- 225 1. This is the first report examining the clinical outcomes after treatment with 0.1%
226 fluorometholone in the very early phase after Small incision lenticule extraction
227 procedure.
- 228 2. Visual and optical recovery of patients that were treated with 0.1%
229 fluorometholone (q1/2h) in the first 2h after Small incision lenticule extraction were
230 significantly improved in the very early postoperative phase.

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232 The authors did not receive any financial support from any public or private sources.

233 **Conflicts of interest**

234 The authors declare that they have no competing interests.

235 **Ethics approval and consent to participate**

236 All interventions approved by the Institutional Review Board of Fujian Medical
237 University (Fuzhou, China), and were conducted according to the principles in the
238 Declaration of Helsinki.

239 **Informed consent**

240 Informed consent was obtained from all individual participants included in the study.

241 **Availability of data and material**

242 All data are available and stored by the authors. If someone wants to request the data
243 from this study, please contact with Zhengwei Shen (E-mail:
244 linqh19870624@163.com)

245 **Consent for publication**

246 Written consent was obtained from the patient for publication of this manuscript and
247 any accompanying images. A copy of the written consent is available for review by
248 the Editor.

249 **Competing interests**

250 The authors declare that they have no competing interests.

251 **Acknowledgements**

252 Not applicable.

253 **Contributions**

254 A. B. and C.D. wrote the main manuscript text and E.F. prepared figures 1. All
255 authors reviewed the manuscript.

256

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301

302

303 **Figure Legends:**

304 Fig 1.Number of eyes recovering higher than 1.0 (logMAR 0.00) among different
305 patient groups.

Figures

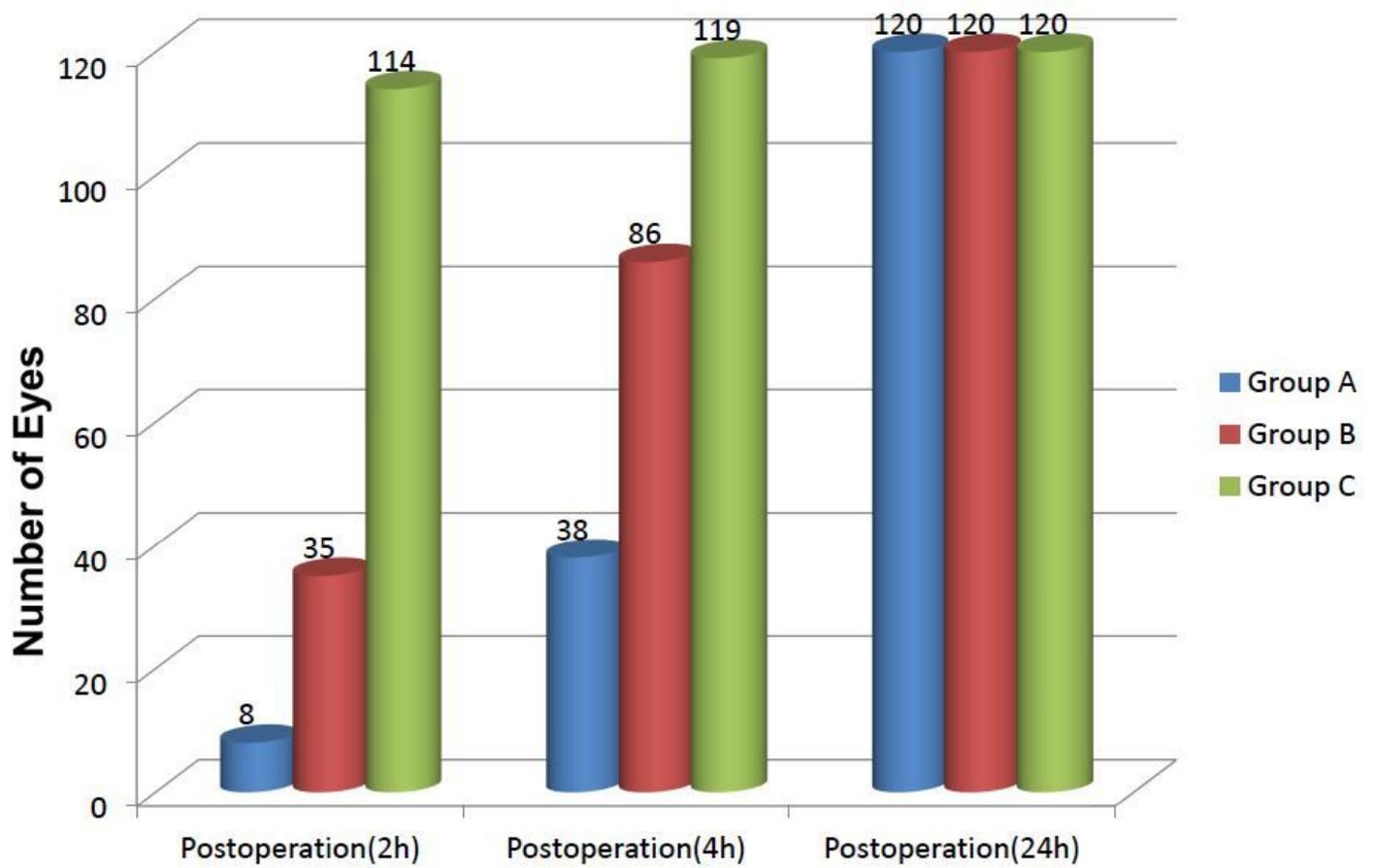


Figure 1

Number of eyes recovering higher than 1.0 (logMAR 0.00) among different patient groups.