We developed a new surgical treatment in which a microneedle is used for retinal endovascular cannulation to treat eyes with central retinal vein occlusion by flushing thrombus out of the central retinal vein as it passes through the lamina cribrosa. The eyes of 12 consecutive patients (12 eyes) with central retinal vein occlusion were successfully treated using this novel treatment. At 24 weeks after surgery, 9 of 12 eyes had gained more than 15 letters in best-corrected visual acuity, and the mean decrease in central foveal thickness was 271.1 μm. Few complications were observed. The microneedle is stiff and sharp enough to facilitate retinal endovascular cannulation in eyes with central retinal vein occlusion. This new technique is a promising treatment of macular edema due to central retinal vein occlusion.

Video available online at www.jamaophth.com

Although central retinal vein occlusion (CRVO) accounts for few retinal vein occlusion cases, it leads to severe vision loss.1-3 Because CRVO is thought to be caused by thrombus within the central retinal vein in the lamina cribrosa, recanalization is a reasonable treatment strategy; however, no endovascular treatment has been established for vascular occlusions in the human retina.4-8 Green et al9 demonstrated that CRVO is caused by thrombus in the central retinal vein. The occlusion of the major outflow channel of the retinal circulation in eyes with CRVO increases venous pressure, and this results in macular edema and hemorrhages. Therefore, thrombus removal or chemical thrombolysis is a reasonable approach to the treatment of CRVO.

In the past, surgeons used special glass cannulas to pierce dilated retinal veins, but the cannulas were too difficult to maneuver because of their transparency or fragility. We developed a novel microneedle having an outer diameter of 50 μm for retinal vessel cannulation.10 Herein, we report the results of a prospective study of eyes with CRVO in which retinal endovascular cannulation was performed using the microneedle.

Methods

Patients

This study adhered to the tenets of the Declaration of Helsinki. The protocol was approved by the local institutional research ethics committees, and the data analysis was performed at the Yokohama City University Medical Center, Yokohama City, Japan. Between March 2010 and February 2011, patients with CRVO were screened for study eligibility. Twelve patients who met the eligibility criteria were included in the study, and their demographic characteristics are summarized in Table 1. The inclusion criteria were clinical and angiographic diagnosis of CRVO less than 12 weeks after the onset of CRVO, central foveal thickness exceeding 300 μm as mea-
sured by optical coherence tomogra-
phy, and best-corrected visual acuity
(BCVA) between 0 and 65 Early Treat-
ment of Diabetic Retinopathy Study let-
ters (Snellen VA equivalents, 20/1000
and 20/50, respectively). The exclu-
sion criteria were glaucoma, retinal or
disc neovascularization, any previous
 treatment of CRVO, vascular retinopa-
thy due to other causes, and intraocu-
lar surgery during the previous 3
months. The primary end point was
change in BCVA at 24 weeks after sur-
gery compared with initial VA. The
BCVA was measured by examiners who
were masked to patient identification.
The secondary end points were surgi-
cal complications, central foveal thick-
ness alteration, and change in the fo-

Table 1. Demographic and Clinical Characteristics of the Patients

<table>
<thead>
<tr>
<th>Patient No./Sex</th>
<th>Age, y, Study Eye</th>
<th>Mean Interval Since CRVO Diagnosis, mo</th>
<th>Glaucoma</th>
<th>Retinal Perfusion Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/67/OS</td>
<td>11</td>
<td>Absent</td>
<td>Intermediate</td>
<td></td>
</tr>
<tr>
<td>2/M/79/OD</td>
<td>9</td>
<td>Present</td>
<td>Intermediate</td>
<td></td>
</tr>
<tr>
<td>3/F/73/OS</td>
<td>4</td>
<td>Absent</td>
<td>Intermediate</td>
<td></td>
</tr>
<tr>
<td>4/M/80/OD</td>
<td>7</td>
<td>Absent</td>
<td>Nonperfused</td>
<td></td>
</tr>
<tr>
<td>5/F/81/OS</td>
<td>11</td>
<td>Present</td>
<td>Intermediate</td>
<td></td>
</tr>
<tr>
<td>6/M/76/OS</td>
<td>9</td>
<td>Present</td>
<td>Nonperfused</td>
<td></td>
</tr>
<tr>
<td>7/M/56/OD</td>
<td>11</td>
<td>Absent</td>
<td>Intermediate</td>
<td></td>
</tr>
<tr>
<td>8/F/67/OS</td>
<td>4</td>
<td>Present</td>
<td>Perfused</td>
<td></td>
</tr>
<tr>
<td>9/M/59/OS</td>
<td>10</td>
<td>Absent</td>
<td>Intermediate</td>
<td></td>
</tr>
<tr>
<td>10/M/83/OD</td>
<td>4</td>
<td>Present</td>
<td>Nonperfused</td>
<td></td>
</tr>
<tr>
<td>11/F/82/OD</td>
<td>3</td>
<td>Absent</td>
<td>Intermediate</td>
<td></td>
</tr>
<tr>
<td>12/M/79/OD</td>
<td>9</td>
<td>Present</td>
<td>Intermediate</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: CRVO, central retinal vein occlusion.

Figure 1. Retinal endovascular cannulation instrument. A, The instrument consists of a 50-µm microneedle and a 10-mL syringe with a viscous fluid injector. B, The microneedle has an outer lumen of 50 µm and is made of stainless steel (top). A 30-gauge needle is shown for comparison (bottom). The scale shows micrometers.

Figure 2. Cannulated vein in an eye with central retinal vein occlusion. A, The microneedle has been inserted into a branch retinal vein, and then the vessel has been slightly pushed toward the optic disc. B, The streamline produced by successful flushing with balanced saline solution can be seen.
veal avascular zone as determined by digital imaging analysis and fluorescein angiography.

**RETNAL ENDOVASCULAR CANNULATION INSTRUMENT**

A fabricated microneedle having an outer diameter of 50 μm and an inner diameter of 20 μm is used to pierce the dilated retinal vein. The microneedle is made of stainless steel and is manufactured by laser assembly (**Figure 1**); it is sharp and stiff enough to pierce microvessels. When the microneedle is connected to a 10-mL syringe containing a distilled solution, the solution can be injected into a vessel. The volume and pressure of the solution injected are proportional to the pressure of the syringe connected to a viscous fluid control system, which is controlled by the surgeon’s pedal.

**SURGICAL TECHNIQUE**

A 25-gauge microincisional vitrectomy system and a vision system (Constellation; Alcon Laboratories) were used to perform all surgical procedures. After displacing the conjunctiva, 4 trocars were inserted at an angle. One of the trocars was used for chandelier illumination with a light source (Brightstar; DORC Company). After performing a core vitrectomy, a posterior vitreous detachment was created, if not already present, and the internal limiting membrane around the macular region was removed. The microneedle was then used to pierce the dilated vein, with a slight loss-of-resistance sensation serving as an indication that it had been pierced, and the solution was slowly injected into the vein at a pressure of about 4 psi. When the solution was injected into the vein through the microneedle, the vessel turned from red to white, and the injection pressure was then gradually increased to 40 psi. A streamlined flow of the solution in the vein was observed when injected at high pressure, and the appearance of the streamline was evidence of successful retinal endovascular treatment (**Figure 2**). The injection was continued for 3 minutes, during which a 0.05-mL volume of solution was injected. A video (entitled Retinal Endovascular Surgery) is available at http://www.jamaophthalmol.com. The video of retinal endovascular cannulation using a microneedle shows successful injection of the solution into the retinal vessel of the eye with CRVO shown in **Figure 2**. After removing the microneedle, we checked to ensure that no bleeding from the vessel had occurred and closed the scleral wounds without injecting gas.

### RESULTS

The BCVA of 9 of 12 patients had improved by more than 15 letters at 24 weeks after surgery compared with the baseline value (**Table 2**). The mean VA had improved by 14.1 letters at 6 weeks, by 15.3 letters at 12 weeks, by 15.3 letters at 18 weeks, and by 16.3 letters at 24 weeks. The preoperative mean BCVA of 29.6 let-

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>BCVA Central Foveal Thickness, µm</th>
<th>Preoperative</th>
<th>Postoperative at 24 wk</th>
<th>Preoperative</th>
<th>Postoperative at 24 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20/200 20/80</td>
<td>671 343</td>
<td>20/200 20/200</td>
<td>540</td>
<td>393</td>
</tr>
<tr>
<td>2</td>
<td>20/250 20/200</td>
<td>689 290</td>
<td>20/250 20/250</td>
<td>593</td>
<td>390</td>
</tr>
<tr>
<td>3</td>
<td>20/100 20/80</td>
<td>601 330</td>
<td>20/100 20/100</td>
<td>599</td>
<td>391</td>
</tr>
<tr>
<td>4</td>
<td>20/250 20/150</td>
<td>731 290</td>
<td>20/250 20/250</td>
<td>529</td>
<td>401</td>
</tr>
<tr>
<td>5</td>
<td>20/60 20/25</td>
<td>693 345</td>
<td>20/60 20/60</td>
<td>528</td>
<td>323</td>
</tr>
<tr>
<td>6</td>
<td>20/1000 20/330</td>
<td>612 289</td>
<td>20/1000 20/1000</td>
<td>523</td>
<td>300</td>
</tr>
<tr>
<td>7</td>
<td>20/250 20/150</td>
<td>528</td>
<td>20/250 20/250</td>
<td>523</td>
<td>300</td>
</tr>
<tr>
<td>8</td>
<td>20/400 20/150</td>
<td>612</td>
<td>20/400 20/150</td>
<td>612</td>
<td>289</td>
</tr>
</tbody>
</table>

Abbreviation: BCVA, best-corrected visual acuity.
The mechanism of this surgical treatment is thought to be elimination of the vascular occlusion by flushing out thrombus, although it is technically impossible to confirm the disappearance of thrombus in the lamina cribrosa. We speculated that our surgical treatment resulted in a reduction in ischemia, an improvement in retinal perfusion, and a suppression of vascular endothelial growth factor production.

Central retinal vein occlusion is associated with severe vision loss, and ischemic CRVO, in particular, has a poor visual prognosis. The multicenter Central Vein Occlusion Study showed that prophylactic panretinal laser treatment is not a beneficial treatment of ischemic CRVO. Although several pharmacological treatment options exist for macular edema associated with CRVO, a substantial proportion of patients with CRVO are left with visual impairment, so retinal vein cannulation may merit inclusion as an option to treat CRVO.

In conclusion, our technique using a microneedle facilitates retinal endovascular cannulation. The surgical procedure may lead to visual improvement in eyes with CRVO and is accompanied by few intraoperative or postoperative complications. Further long-term follow-up observations and studies are needed to confirm the efficacy of this treatment.

Submitted for Publication: September 11, 2012; final revision received November 19, 2012; accepted November 27, 2012.

Correspondence: Kazuki Kadonosono, MD, Department of Ophthalmology, Yokohama City University Medical Center, Urafune-cho 4-57, Minami-ku, Yokohama 232-0024, Japan (kado@med.yokohama-cu.ac.jp).

Conflict of Interest Disclosures: None reported.


REFERENCES