SURGEON'S CORNER

Endovascular Cannulation With a Microneedle for Central Retinal Vein Occlusion

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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.

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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 al[9] 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.

Video available online at www.jamaophth.com

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 frangibility. 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.

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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-

Table 1. Demographic and Clinical Characteristics of the Patients

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

Abbreviation: CRVO, central retinal vein occlusion.

sured by optical coherence tomography, and best-corrected visual acuity (BCVA) between 0 and 65 Early Treatment of Diabetic Retinopathy Study letters (Snellen VA equivalents, 20/1000 and 20/50, respectively). The exclusion criteria were glaucoma, retinal or disc neovascularization, any previous treatment of CRVO, vascular retinopathy due to other causes, and intraocular surgery during the previous 3 months. The primary end point was change in BCVA at 24 weeks after surgery compared with initial VA. The BCVA was measured by examiners who were masked to patient identification. The secondary end points were surgical complications, central foveal thickness alteration, and change in the fo-

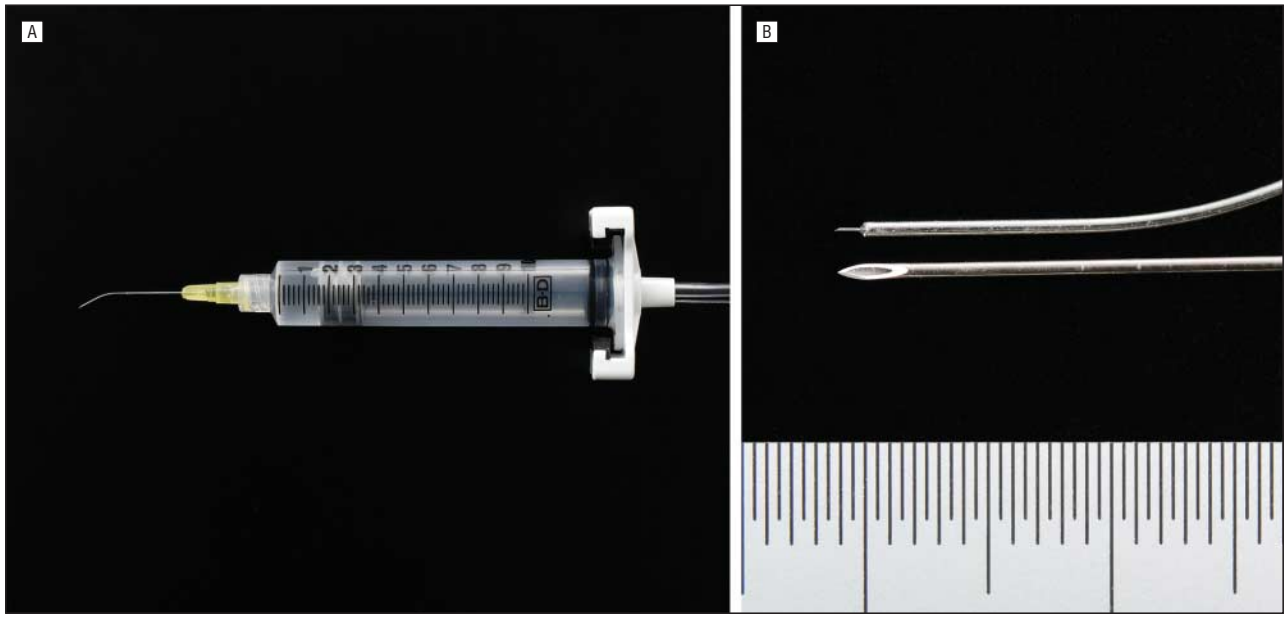

Figure 1. Retinal endovascular cannulation instrument. A, The instrument consists of a 50-µm microneedle and a 10-mL syringe with a viscous fluid injector. B, The microneedle has an outer lumen of 50 µm and is made of stainless steel (top). A 30-gauge needle is shown for comparison (bottom). The scale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

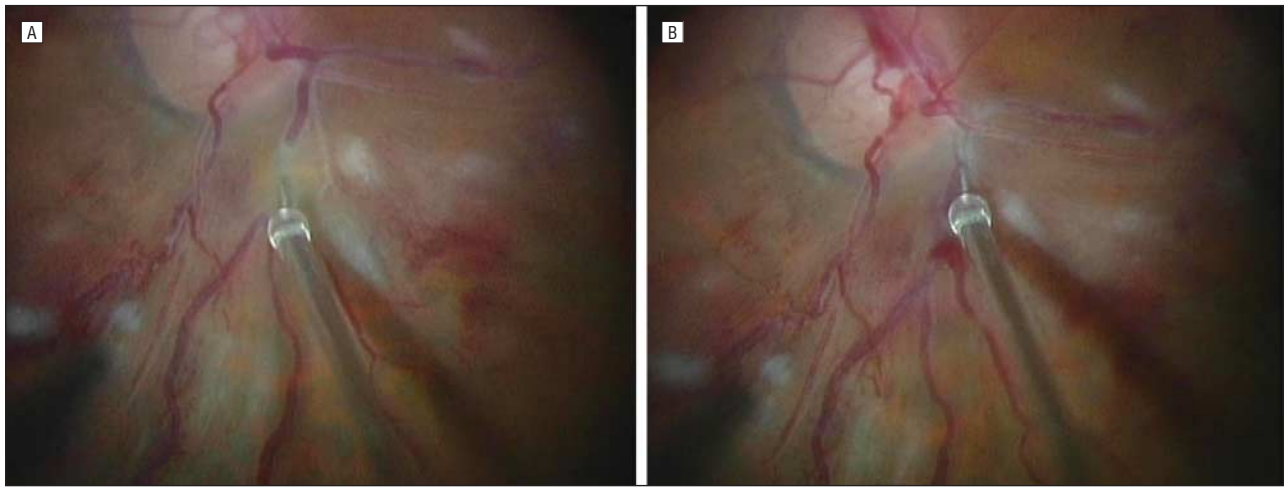

Figure 2. Cannulated vein in an eye with central retinal vein occlusion. A, The microneedle has been inserted into a branch retinal vein, and then the vessel has been slightly pushed toward the optic disc. B, The streamline produced by successful flushing with balanced saline solution can be seen.

veal avascular zone as determined by digital imaging analysis and fluorescein angiography.

RETINAL 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.

Table 2. Surgical Outcome

Patient No.	BCVA		Central Foveal Thickness, μm	
	Preoperative	Postoperative at 24 wk	Preoperative	Postoperative at 24 wk
1	20/200	20/80	671	343
2	20/250	20/80	540	393
3	20/500	20/200	689	290
4	20/1000	20/250	593	390
5	20/100	20/80	601	300
6	20/500	20/100	599	391
7	20/250	20/150	529	401
8	20/60	20/25	693	345
9	20/100	20/330	528	323
10	20/500	20/200	731	290
11	20/250	20/150	523	300
12	20/400	20/150	612	289

Abbreviation: BCVA, best-corrected visual acuity.

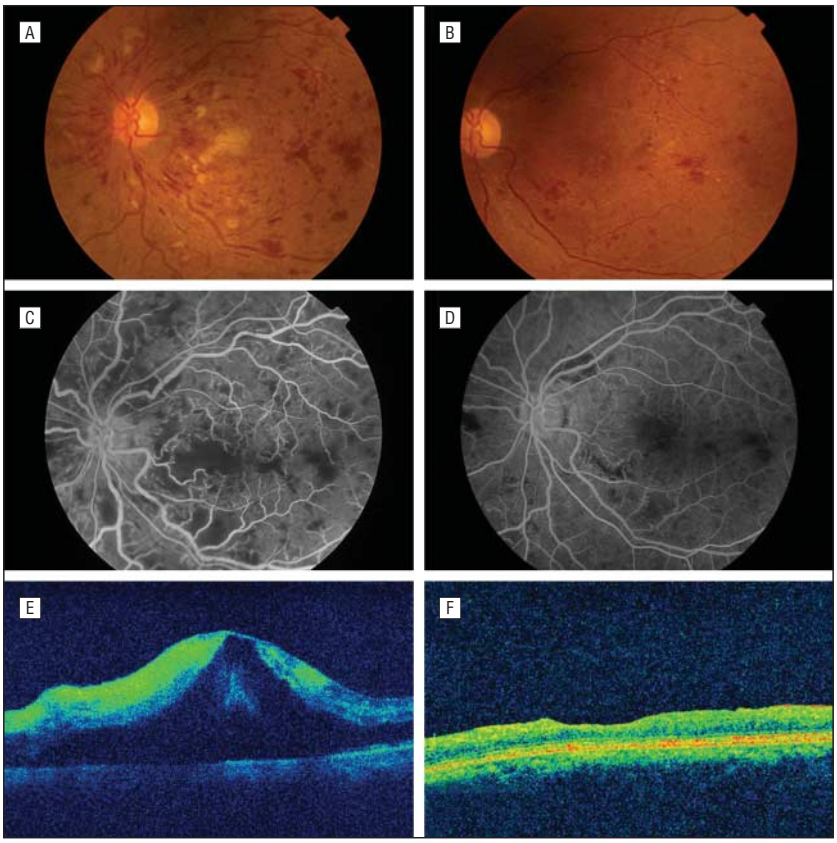

Figure 3. Fundus photographs, angiographic images, and optical coherence tomography images of the eye in patient 3 with central retinal vein occlusion before and after endovascular treatment. The retinal hemorrhages and soft exudates observed before surgery (A) have decreased markedly at 6 weeks after surgery (B). Comparison with the preoperative fluorescein angiographic image (C) shows less dilated retinal veins, improvement in vascular leakage, and reconstructed macular vasculature (D). A decrease in the avascular area and the presence of a perifoveal capillary network are seen at 6 weeks after surgery. The postoperative optical coherence tomography image (F) shows a marked decrease in macular edema compared with the preoperative optical coherence tomography image (E).

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-

ters (20/250) had improved to 45.9 letters (20/125) at 24 weeks after surgery, and the mean decrease in central foveal thickness was 271.1 μm (**Figure 3**).

No neovascular glaucoma was observed in any of the patients when examined at 24 weeks. All surgical procedures were successful, as confirmed by the streamlined flow during the injection. Intraoperative complications developed in 2 patients and consisted of a mild vitreous hemorrhage in 1 eye and a small subretinal hemorrhage in 1 eye, neither of which impaired VA. No occurrences of retinal tears, endophthalmitis, retinal detachment, severe vitreous hemorrhage, or recurrence of macular edema were observed during the 24-week follow-up period.

DISCUSSION

We demonstrated that retinal endovascular cannulation performed by piercing the retinal vein and injecting saline solution through a microneedle is a feasible treatment of CRVO and is unaccompanied by any severe surgical complications. The microneedle we used is made of stainless steel and has an outer lumen of 50 μm and an inner lumen of 20 μm. Modern industrial technology has made it possible to fabricate needles with a tiny lumen by laser assembly. Based on the favorable results obtained in an experimental study[10] of the feasibility of using the microneedle, it was applied to human retinal veins. With the microneedle, all eyes with CRVO were successfully treated in this study, without any severe intraoperative complications.

At the 24-week follow-up examination, 9 of 12 eyes had gained more than 15 letters in VA, and the mean change in all 12 eyes at 24 weeks was an increase of 16.3 letters. Because visual improvement is rarely observed during the natural course of ischemic CRVO,[11] we consider the high rate of visual improvement and the low rate of surgical complications achieved using our technique in this study to be satisfactory.

The mechanism of this surgical treatment is thought to be elimination of the vascular occlusion by flushing out thrombus,[12] 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.[2,3] The multicenter Central Vein Occlusion Study[13] 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,[14-17] 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.

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Conflict of Interest Disclosures: None reported.
Online-Only Material: A video is available at http://www.jamaophth.com.

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