Lamina Puncture

Pars Plana Optic Disc Surgery for Central Retinal Vein Occlusion

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Objective: To determine the feasibility of creating a perivascular space adjacent to the central retinal vein at the level of the lamina cribrosa as a potential method of re-establishing perfusion in central retinal vein occlusion.

Methods: Various designs for a puncture instrument, or lamina puncture lancet, were investigated in cadavers, pigs that had undergone enucleation, and in vivo rabbit eyes.

Results: A lancet with a sharp cutting edge on one side and an opposing blunt edge is repeatedly able to create a perivascular space with limited optic nerve fiber damage.

Conclusions: Lamina puncture is technically feasible, and evaluation in carefully selected patients appears warranted.

Arch Ophthalmol. 2002;120:495-499

Central retinal vein occlusion (CRVO) remains a difficult and often frustrating disease for both the patient and the ophthalmologist. Although some younger patients with nonischemic forms may recover, most patients with CRVO are left with poor vision; in patients with widespread capillary non-perfusion, less than 10% maintain a visual acuity better than 20/400 OU.1 No treatment has proved useful in improving vision, and ophthalmic care is supportive with observation for the development of iris neovascularization and the need for intervention with retinal ablation.2

Histological studies suggest that regardless of the level of perfusion, most or all cases of CRVO result from thrombus formation in the central retinal vein at or just posterior to the lamina cribrosa.3 Anatomically, the luminal diameter of the central retinal vein is narrowest at this level, resulting from the relatively denser connective tissue that makes up the lamina cribrosa encircling the retinal vessels. The development of CRVO is undoubtedly multifactorial, including the resultant increased turbulence in blood flow, possible concomitant endothelial cell damage, and possible systemic factors, and results in a wide variety of CRVO forms with variable degrees of perfusion. Nevertheless, the mechanical constriction of the central retinal vein at the lamina cribrosa predisposes this location to thrombus formation.

We postulated that it might be possible to restore normal perfusion to the central retinal vein if a surgical technique could be developed to release the constriction of the central retinal vein by the surrounding connective tissue at the level of the lamina cribrosa. The resulting increase in luminal diameter of the central retinal vein might allow the passage of a thrombus. Alternatively, the increased intraluminal diameter might permit sufficient blood flow at the level of the lamina cribrosa to allow for increased perfusion of the retina, even if the thrombus was not dislodged or expressed mechanically.

We tried to determine the feasibility of transvitreal optic disc surgery to create a perivascular opening in the lamina cribrosa, which we termed lamina puncture, as a prelude to considering such an intervention in patients with CRVO.

MATERIALS AND METHODS

Initial experiments were performed on human cadaver eyes and enucleated pig eyes; the latter were chosen for their anatomical similarity to human eyes. Lamina puncture was performed in enucleated eyes after removing the anterior segment, including both the vitreous and the vitreous base. This preparation permitted direct visualization of the posterior eye cup and optic...
Subsequent experiments used intact Dutch-belted rabbits in a transvitreal approach. These experiments were reviewed and approved by the animal review committee at our hospital. After anesthesia with 3 to 5 mL of a mixture (1:1) of intramuscular ketamine hydrochloride (100 mg/mL) and xylazine hydrochloride (20 mg/mL), the animals were placed under a dissecting microscope, and adequate anesthesia was confirmed. Following a localized peritomy, a 1.5-mm superior sclerotomy was performed approximately 1.5 mm posterior to the limbus. The lamina puncture lancet was introduced through this sclerotomy without removal of the vitreous. A contact lens and operating microscope were used for visualization and illumination. The various lancets were moved across the vitreous and into the optic disc. The rabbits were euthanized, and the eyes were enucleated after 3 to 4 minutes of observation for hemorrhage and confirmation of retinal vascular perfusion. All tissues were processed for light microscopy using conventional techniques.

The instruments were initially shaped from copper and molten glass. These 2 materials were selected for their ductility, relative strength, and ability to be used in areas with small dimensions, all of which facilitated frequent early changes.

Subsequent modifications were refined on instruments made of surgical stainless steel. Lamina puncture lancets were evaluated for each instrumental design on the basis of the following parameters: the ability to create a perivascular space around the central retinal vein, the presence and degree of damage to the vessel wall, the amount of residual connective tissue adjacent to the vessel wall, and the amount of damage done to nerve fibers.

RESULTS

Initial experiments on enucleated eyes were encouraging because the vessel wall of the central retinal vein appeared to be much stronger than the connective tissue fibers of the lamina cribrosa, and consequently it was possible to selectively disrupt the lamina cribrosa without violating the integrity of the central retinal vein. Although blunt lamina puncture lancets in combination with multiple passes and a slightly roughened surface were very effective in stripping away connective tissue from around the central retinal vein, these instruments caused significant collateral damage to the optic nerve fiber tissue (Figure 1). Puncture instruments with a sharp cutting edge were superior to blunt instruments in minimizing the area of damage to optic nerve fibers, but this cutting edge created damage in the central retinal vein wall if directed against the vessel (Figure 2).

As a result, puncture instruments were created that combined a slightly roughened blunt side with a cutting edge on the opposite side. These lancets were passed through the optic nerve head with the cutting edge directed away from the vessel wall. This design required little force to allow a relatively small puncture to be made through the lamina cribrosa, especially when the instrument was angled so that the cutting edge entered the nerve head first. At the same time, the roughened blunt side did not damage the vein wall and was able to completely strip away the connective tissue of the
lamina cribrosa from the vessel wall with only a few consecutive passes. This final version was 300 to 400 µm in width, with a sharp portion about 60 µm in length and a relatively blunt tip (Figure 3). The shaft diameter was equivalent to 20 gauge, allowing it to be passed through a standard sclerotomy. Small (300- to 400-µm diameter) puncture wounds were achievable immediately adjacent to the vessel walls, with no wall damage and minimal optic nerve fiber damage (Figure 4).

This final lancet design was then used to create lamina punctures in 8 consecutive in vivo rabbit eyes. In 7 of the 8, there was no bleeding and grossly normal perfusion after the puncture. The vein wall was intact on histological examination in all cases (Figure 5). In the sole eye in which there was bleeding, the amount of blood was minimal, and hemostasis occurred spontaneously after about 20 seconds. Although the central retinal vein was intact on histological examination, a small branching vessel on the optic disc had been severed, accounting for the hemorrhage.

**COMMENT**

Although many questions may be raised about the possibility of effective therapy for an acutely compromising event such as CRVO, the development of a thrombus at the site of constriction by the lamina cribrosa appears central to this disease. Consequently, attempts to relieve vascular compromise and restore blood flow are consistent with the underlying pathophysiologic characteristics of CRVO. Lamina puncture may relieve constriction on the central retinal vein and permit thrombus migration or bypass by creating a potentially enlarged vascular diameter. Furthermore, it is also possible that mechanical compression of the vein during the procedure might result in clot dislodgment unrelated to vascular diameter, but this mechanism cannot be evaluated from the available animal models.

In addition to other concerns regarding the visual efficacy of reestablishing blood flow by any means, 2 potential limitations to lamina puncture are the failure of the technique to reestablish perfusion and the possibility of excessive collateral optic nerve damage. The latter seems unlikely, however, given the anatomy of the optic nerve head. Macular fibers enter the optic nerve head along the periphery. With the puncture adjacent to the central retinal vein and with damage therefore limited to the central portion of the nerve, it seems reasonable that any reduction in central vision associated with the puncture would be minimal. Furthermore, for CRVO in patients older than 65 years, the extremely poor natural history for visual recovery suggests that optic nerve head trauma would not be a significant limiting factor in the initial evaluation of the procedure. Until further in vivo experiments are performed, it is not possible to determine if releasing constriction of the central retinal vein at the level of the lamina cribrosa will allow for mobilization of the thrombus and reperfusion of the retina.

There have been many previous attempts to develop treatments for CRVO. Early approaches such as the use of cholesterol-lowering agents' or x-rays' did not take into account the cause of the disease; namely, the for-
mation of a thrombus at the level of the lamina cribrosa. More recent approaches have been based on this pathogenesis.

Rather than reperfusion of the retina via the central retinal vein, McAllister, Vijayasekaran, et al,6,8 created a new venous outflow route by forming a chorioretinal venous anastomosis through the use of high-energy argon lasers. They showed the feasibility of such anastomosis in both dog and rat models. McAllister and colleagues showed that similar chorioretinal venous anastomosis could be created in 8 of 24 patients in a small pilot study. Encouragingly, in those 8 patients, not only was retrograde venous flow demonstrated with some degree of visual improvement, but the anastomosis seemed to remain patent for the duration of the study, ranging from 1 to 3 years. Although approximately 40% of the sites with attempts at anastomosis creation developed hemorrhages, these were all visually insignificant and resolved spontaneously. Nevertheless, the potential for a significant hemorrhage exists, as does the development of preretinal and subretinal fibrosis. A larger multicenter trial is under way to determine the efficacy of this treatment. The fact that the limited reperfusion achieved in the 33% of patients in whom an anastomosis could be successfully created was associated with visual improvement, whereas not statistically significant, is encouraging for our current study. It suggests that if lamina puncture is successful in improving retinal venous outflow, there is the potential for visual improvement.

Thrombolytic agents are also used to dissolve a thrombus at the level of the lamina cribrosa. Early studies using systemic streptokinase9 showed statistically improved vision in patients who were taking the drug. However, in 3 of 20 patients, severe vitreous hemorrhage occurred leading to functional blindness. A more recent study used tissue-type plaminogen activator (tPA), which has a better safety profile than streptokinase, has a shorter circulating half-life, is less antigenic, and carries less risk of creating a fibrinolytic state leading to significant systemic hemorrhage. A pilot study using tPA by Elman10 in 1996 had encouraging results. Fifty-nine percent of the 89 patients with sufficient follow-up (of an original 96 patients) had 3 or more lines of visual improvement. However, 3 patients developed intraocular bleeding, and 1 patient had a fatal hemorrhagic stroke. A decreased risk of extraocular hemorrhage might be achieved with localized delivery of tPA via retinal vein cannulation. Weiss11 showed that this is technically feasible and was able to achieve modest improvement in 4 of 8 eyes, with no catastrophic adverse effects.

Although pharmacologic dissolution of a thrombus may restore blood flow, this therapeutic strategy does not relieve the constriction of the central retinal vein at the level of the lamina cribrosa. In addition, endo-}

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**Figure 5.** The optic nerve in an in vivo rabbit eye after lamina puncture using the final instrument design. There is little collateral tissue damage with an intact vessel wall (hematoxylin-eosin; original magnification × 20).
side and a roughened blunt side placed adjacent to the central retinal vein was repeatedly able to produce a significant perivascular space with limited collateral nerve fiber damage. Although the potential efficacy and complications of this procedure in patients with CRVO are unknown, our study’s promising results and the dismal visual prognosis in certain subgroups of patients with CRVO suggest that lamina puncture should be evaluated in a select group of patients.

Submitted for publication October 11, 2001; final revision received January 6, 2002; accepted January 18, 2002.

Supported in part by the Vitreo-retinal Research Fund (Dr D’Amico), Boston, Mass.

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REFERENCES


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