

# EAGLE to Study Central Retinal Artery Occlusion

The natural course of central retinal artery occlusion often leads to blindness in the affected eye.

BY CONNI BERGMANN KOURY, EDITOR-IN-CHIEF

**T**he Multicenter Study of the European Assessment Group for Lysis in the Eye (EAGLE) is the first randomized prospective clinical trial to compare conservative medical treatment and local intraarterial fibrinolysis (LIF) in patients with central retinal artery occlusion (CRAO). According to a report in *Graefes Archives of Clinical Experimental Ophthalmology*, “the results of this study should enable ophthalmologists and neuroradiologists to improve the therapy of patients with acute CRAO.”

As of yet, no conservative study for CRAO to date has proved effective in retrospective studies, wrote Nicolas Feltgen, MD, and colleagues; therefore, in 1991, physicians began using LIF among patients with acute CRAO. The researchers said that the therapy is similar to minimally invasive therapy used in patients with acute ischemic stroke. It showed promise in pilot studies when compared with conservative treatment, leading to investigation in a randomized multicenter study.

The EAGLE trial, begun in 2002, is evaluating the therapeutic efficacy of LIF. To be included, patients must be aged between 18 and 75 years, have a CRAO not older than 20 hours with visual acuity <0.32. According to the investigators, the most important exclusion criteria are branch retinal artery occlusion, cilioretinal artery supplying the macula and serious general disease, Dr. Feltgen and colleagues wrote.

After randomization, patients are treated with conservative measures (ie, bulbus massage, lowering intraocular pressure with topical beta-blocker and acetazolamide acetylsalicyclic acid, heparin and isovolemic hemodilution [depending on the hematocrit]) (Table 1). Patients who are assigned LIF will receive a

TABLE 1. METHODS OF TREATMENT	
Conservative Standard Treatment	Local Intraarterial Fibrinolysis (LIF)
IV injection of heparin	IV injection of heparin
IV injection of acetazolamide	LIF
Globe massage	
Topical use of a beta-blocker	
Isovolemic hemodilution	
Acetylsalicyclic acid	

maximum of 50 mg recombinant tissue plasminogen activator (rTPA) injected into the ophthalmic artery by a neuroradiologist. During the following 5 days, all patients are treated with heparin.

## BACKGROUND

The primary endpoint of the study is visual acuity 1 month following therapy compared with baseline visual acuity. The calculated sample size is 100 patients per sub-trial, for a total of 200 patients.

As of August, 68 patients were included, and treatment is only justified in randomized multicenter studies because of the limited therapeutical visual outcome. The authors wrote, “We welcome new study centers to join.”

The annual incidence of all newly diagnosed CRAO is about one to 15 per 10,000 people; for acute CRAO, fewer than one case per 100,000 is reported. Most patients are aged between 65 and 70 years and

**TABLE 2. STUDY CENTERS**

- Aachen (Germany)
- Bern (Switzerland)
- Bonn (Germany)
- Essen (Germany)
- Freiburg (Germany)
- Hamburg/Altona Eye Hospital (Germany)
- Hamburg/University Eye Hospital (Germany)
- Hannover (Germany)
- Homburg/Saar (Germany)
- Innsbruck (Austria)
- Kiel (Germany)
- Lubeck (Germany)
- Mainz (Germany)
- Munich/University Eye Hospital (Germany)
- Vienna (Austria)
- Wurzburg (Germany)

have atherosclerotic disease. According to Dr. Feltgen and colleagues, surgeons have used many strategies to improve visual acuity among these patients. So-called conservative treatments include topical beta-blockers, acetylsalicylic acid, globe massage, isovolemic hemodilution, heparin, pentoxifylline, anterior chamber paracentesis and the use of carbogen therapy. These therapies have a success rate of about 15%.

LIF has a better success rate in the literature, however, most of these studies included few patients and were nonrandomized and retrospective. Dr. Feltgen wrote that from a theoretical point of view, LIF is the most convincing therapy because of its causal treatment. "The rationale of LIF rests on the assumption that the damage caused by retinal ischemia is reversible within a short time interval after the CRAO. Yet thromboembolic complication is a rare but possible side effect."

EAGLE investigators are evaluating LIF for CRAO based on one primary and four secondary outcomes. The primary endpoint is the change in visual acuity from initial examination to follow-up 1-month after CRAO using letter-by-letter scoring on the Early Treatment of

Diabetic Retinopathy Study (ETDRS) chart. The secondary endpoints are:

- Change in visual fields using Goldmann's kinetic perimetry;
  - The influence of the therapies on retinal circulation as seen on fluorescein angiography;
  - Safety of the two procedures and number, type and grade of complications; and
  - Monitoring the prognostic importance of the (1) time between onset of CRAO and start of therapy, (2) the grade of CRAO and (3) preexisting systemic diseases.
- Each patient will be examined at six visits, during the first 5 days after treatment and 1 month after treatment.

### LOCAL INTRAARTERIAL FIBRINOLYSIS

The procedure begins with the femoral artery punctured under local anesthesia and a guiding catheter introduced and advanced to the bifurcation of the carotid artery, according to the report. An angiography is performed, and the catheter is moved forward to the proximal, extracranial part of the internal carotid artery. To prevent thrombosis, a continuous arterial saline flush is attached to the guiding catheter. Anticoagulation is controlled using heparin. A superselective microcatheter is introduced coaxially through the guiding catheter into the ophthalmic artery. LIF is terminated after a maximum of 50 mg of the rTPA Actilyse (Boehringer Ingelheim GmbH, Ingelheim, Germany).

Following injections of 15, 30, 45 and 50 mg, the ophthalmologist performs a Snellen test of visual acuity and a direct funduscopy to evaluate retinal changes. Patients are also treated with low-dose heparin twice daily for 5 days, and neurological and cardiological exams are performed.

The trial is being carried out according to the intention-to-treat principle, Dr. Feltgen and colleagues wrote. "CRAO is an ocular emergency," the authors said. "LIF is a promising treatment, but there is currently insufficient evidence to justify LIF as a standard therapy." The trial is suffering from sluggish enrollment, the authors said. They ask that, when able, ophthalmologists transfer eligible patients immediately before any treatment to one of the study centers (Table 2). ■

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