

Combined endoscope-assisted procedures (CEaP) for the management of neovascular glaucoma

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Title: Combined Endoscope-Assisted Procedures (CEaP) for the Management of Neovascular Glaucoma

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Abstract:

Background: Neovascular glaucoma (NVG) is a severe and vision-threatening form of secondary glaucoma characterized by both retinal ischemia and elevated intraocular pressure (IOP). Effective management requires simultaneous control of the ischemic stimulus and IOP. However conventional cyclodestructive techniques are associated with significant risks including severe inflammation, hypotony and phthisis bulbi. This study aimed to evaluate the efficacy and safety of a combined surgical approach—endoscopic cyclophotocoagulation (ECP), pars plana vitrectomy (PPV), and panretinal photocoagulation (PRP)—for treating neovascular glaucoma (NVG).

Methods: This retrospective, non-comparative interventional case series included 30 eyes from 30 patients treated at a tertiary referral care center in France. The primary outcome was mean intraocular pressure (IOP) reduction. Secondary outcomes included changes in best-corrected visual acuity (BCVA), pain levels, antiglaucoma medication use, and postoperative complications.

Results: The mean IOP decreased from 41.77 ± 9 mmHg preoperatively to 16.2 ± 8.1 mmHg at one month and 15 ± 9.35 mmHg at six months ($p < 0.0001$). Pain levels and the number of antiglaucoma medications significantly decreased at 1 month ($p < 0.0001$ and $p = 0.00046$, respectively). BCVA remained stable (2.26 to 2.37; $p = 0.116$), indicating preserved visual function. No intraoperative complications occurred. Early postoperative complications included transient corneal edema (13.3%), hyphema (16.7%), uveitis (20%), hypotony (6.7%), and others, all resolving without long-term sequelae. No severe adverse events were reported.

Conclusions: This combined surgical technique appears safe and effective and may represent a promising early interventional strategy for NVG, significantly reducing IOP and treatment burden in a high-risk patient population.

Key words

Combined surgery; Cyclodestruction; Endocyclophotocoagulation; Glaucoma; Intraocular pressure; Neovascular glaucoma; Retinal ischemia

Background

Neovascular glaucoma (NVG) is a challenging and vision-threatening subtype of secondary glaucoma, marked by the growth of abnormal blood vessels across the iris surface and within the anterior chamber angle. This neovascularization obstructs aqueous humor outflow, resulting in a progressive rise in intraocular pressure (IOP)[1]. NVG is most frequently triggered by severe retinal ischemia and is commonly associated with underlying conditions such as central retinal vein occlusion, proliferative diabetic retinopathy, central retinal artery occlusion, and carotid artery occlusion[2].

Effective management of NVG requires a dual approach targeting both the ischemic stimulus and the IOP elevation. Therapeutic strategies may include panretinal photocoagulation (PRP), intravitreal anti-VEGF therapy, anterior retinal cryotherapy (ARC), filtering surgeries, and cyclodestructive interventions like cyclocryotherapy (CCT) and transscleral cyclophotocoagulation (TSCPC)[1, 3]. While effective at lowering IOP, traditional cyclodestructive techniques are associated with significant risks including severe inflammation, hypotony and phthisis[4, 5].

Endoscopic cyclophotocoagulation (ECP) has emerged as a more advanced cyclodestructive technique[6]. By integrating laser delivery with endoscopic visualization in a single probe, ECP enables real-time imaging of the ciliary processes, allowing for more selective tissue ablation and reduced collateral damage[6].

A combined approach incorporating endoscopic cyclophotocoagulation and pars plana vitrectomy, referred to as ECP-plus, along with endoscopic panretinal photocoagulation—collectively termed Combined Endoscope-Assisted Procedures (CEaP)—has been reported as an effective and safe intervention for neovascular glaucoma[7, 8].

In this study, we evaluate the efficacy and safety of the CEaP for the treatment of neovascular glaucoma.

Material and Methods

A retrospective study was conducted by reviewing clinical data from patients who visited a tertiary referral center, Aix Vision in Aix-en-Provence, France, between March 2018 and September 2023. Written informed consents for the use of clinical records was obtained from all participants. All patient data were anonymized before analysis. The study was approved by the Ethics Committee of the French Society of Ophthalmology (IRB 00008855, Société Française d'Ophtalmologie IRB#1) and was in accordance with the Declaration of Helsinki.

Inclusion and Exclusion Criteria

Patients were included if they had a diagnosis of neovascular glaucoma (IOP > 21 mmHg with neovascularization in the anterior chamber angle and iris). Exclusion criteria included prior glaucoma filtering surgery, glaucoma drainage devices, ARC, CCT, or TSCPC, inadequate follow-up, or absence of lens extraction. **Therefore, all included eyes were pseudophakic.**

Clinical Assessment and Outcomes

IOP was measured using Goldmann applanation tonometry by a trained ophthalmologist. Baseline IOP was recorded at the time of neovascular glaucoma diagnosis, while postoperative IOP was assessed at 1, 6, and 12 months by the referring ophthalmologist.

The primary outcome was mean IOP reduction at 6 months, evaluated by absolute IOP values and percentage reduction. Secondary outcomes included changes in visual acuity (VA), pain level, number of antiglaucoma medications, and postoperative complications.

Intervention

All surgeries were performed by a single surgeon (SG). Surgeries were performed under monitored anesthesia care with retrobulbar anesthesia of 3mL of xylocaine 2% and naropaine 7,5mg with or without intravenous sedation. Tropicamide 0.5% and Mydriastert were used for pupil dilatation. A 3 port (two 25G sclerotomies and one 20G sclerotomy) pars plana vitrectomy was performed. During vitrectomy, 360-degree PRP was applied from the equatorial region extending to the ora serrata.

Following vitrectomy, a 19G ECP probe was then introduced through the 20G sclerotomy into the posterior segment. Visualization of the pars plana and ciliary processes was achieved via a high-resolution external monitor. ECP was applied over 270-degree of the ciliary body circumference, using a laser power of 120-150 mW with exposure duration of 0,15-0,2 seconds, modulated continuously by the surgeon. The treatment endpoint was defined by a visible whitening and shrinkage of the ciliary processes. At the

conclusion of the procedure, instruments were withdrawn and sclerotomies were sutured closed with vicryl rapid 8/0.

An intravitreal injection of aflibercept 2mg/0.05mL was administered intraoperatively, at the end of the procedure to reduce the risk of bleeding from residual neovascular tissue. Anti-VEGF was not used postoperatively. Routine preoperative anti-VEGF was not part of our standard protocol to avoid delaying definitive surgical treatment.

Perioperative medications included a subconjunctival injection of 0.1mL of dexamethasone, subtenon injection of ropivacaine topical Atropine 1% drops and topical tobramycin-dexamethasone ointment (Figure 1; see Video, Supplemental Digital Content 1). Patients were instructed to continue their pre-existing antiglaucoma therapy during the early postoperative period. In addition, they were prescribed topical antibiotics to be instilled four times daily for 7 to 10 days, prednisolone acetate 1% every 1 to 2 hours while awake, and a nonsteroidal anti-inflammatory agent applied two to three times per day. The tapering of corticosteroids, anti-inflammatory and glaucoma medications was guided by the clinical course, particularly intraocular pressure control and the degree of anterior segment inflammation. The endoscopic system used was the Endo Optiks® E2 Laser (BVI, Endo Optiks, Inc., Little Silver, NJ, USA).

Patients were followed at 1, 6, and 12 months postoperatively. Postoperative complications were recorded, including hypotony (IOP < 5 mmHg for >2

weeks), hyphema, severe uveitis, corneal oedema, endophthalmitis, and retinal detachment.

Definition of Treatment Success

Treatment success was defined as IOP between 5 and 21 mmHg without additional intervention. Antiglaucoma medications were prescribed if IOP exceeded 21 mmHg at any follow-up visit.

Statistical Analysis

Preoperative and postoperative IOP values were compared using the Friedman test. **Post-hoc pairwise comparisons following the Friedman test were not performed; only the result of the global test is reported. Kaplan-Meier survival analysis was not performed because of the retrospective design, the limited sample size, and the substantial loss to follow-up at 12 months. Cumulative success rates at each follow-up visit were instead calculated as the proportion of eyes meeting the success criterion among those with available data at that time point (available-case analysis); missing data were not imputed.** Changes in best-corrected visual acuity (BCVA), pain level, and number of antiglaucoma medications were analyzed using the nonparametric Wilcoxon signed-rank test. A p-value < 0,05 was considered statistically significant.

Results

Study population

Thirty eyes from 30 patients were included in the study. The mean age of the study population was $78 \pm 13,85$ years. The cohort comprised 63,33% men and 36,67% women. The underlying etiologies of neovascular glaucoma were central retinal vein occlusion in 18 patients (60%), central retinal artery occlusion in 5 patients (16.67%), proliferative diabetic retinopathy in 2 patients (6.67%), branch retinal vein occlusion in 1 patient (3.33%), and ocular melanoma in 1 patient (3.33%), while data were unavailable for 3 patients (10%) (Table 1). The patient with ocular melanoma had a previously diagnosed and treated choroidal melanoma managed with plaque brachytherapy, CEaP was therefore performed only once tumor control had been confirmed. For the 3 patients with unavailable etiology data, the underlying retinal disease could not be retrospectively determined because of an incomplete referral records ; an undetermined etiology is similarly reported in 19-21% of eyes in comparable neovascular glaucoma cohorts.[9] Follow-up data were available for 30 eyes at 1 month, 28 eyes at 6 months, and 16 eyes at 12 months; the 12-month analysis included all 16 eyes with available data at that time point.

The mean operative time for the 30 procedures was 47 minutes (± 20). For the 10 most recent procedures, the mean operative time decreased to 31,7 minutes (± 6.3).

IOP Outcomes

Preoperative IOP ranged from 25 to 55 mmHg, with a mean of $41,77 \pm 9$ mmHg. Postoperatively, mean IOP was $16,2 \pm 8,1$ mmHg at 1 month and $15 \pm 9,35$ mmHg at 6 months (Table 2). This corresponded to an IOP reduction of 58% at 1 month and 62% at 6 months, with statistical significance ($p < 0,0001$).

Visual Acuity and Pain Assessment

The mean preoperative BCVA was 2,26 ($\pm 0,753$) logMAR (Hand Motion (HM)), and the mean postoperative BCVA was 2,37 ($\pm 0,699$) logMAR (HM). VA remained stable or improved in 15 patients, with no statistically significant difference between preoperative and postoperative values ($p = 0,116$).

Pain levels, assessed using the Visual Analog Scale (VAS, ranging from 0: « no pain » to 10: « worst pain »), showed a significant reduction at 1 month. The mean preoperative VAS score was 3,57, decreasing to 0,27 at 1 month postoperatively ($p < 0,0001$). Pain was assessed only at 1 month postoperatively, as VAS scores were systematically recorded at the early

postoperative visit but were not routinely documented by the referring ophthalmologists who conducted the 6- and 12-month follow-up visits.

Medication Use

Seventeen patients required acetazolamide preoperatively, whereas none required it postoperatively. The mean number of hypotensive drops significantly decreased from 2,69 to 1,67 ($p = 0,00046$).

Complications

No intraoperative complications were reported. Postoperatively, complications included:

- Corneal edema (4 patients, 13,3%)
- Hyphema (5 patients, 16,7%)
- Intravitreal hemorrhage (1 patient, 3%)
- Exudative retinal detachment (1 patient, 3%)
- Anterior fibrinous uveitis (6 patients, 20%)
- Prolonged hypotony (IOP < 5 mmHg for >2 weeks) (2 patients, 6,7%)

All postoperative complications were resolved with appropriate treatment. No cases of endophthalmitis, phthisis bulbi, or other severe complications were observed (Table 2).

Discussion

CEaP is an emerging surgical technique that addresses both retinal ischemia and IOP elevation in a single procedure[6]. In our study, we utilized endocyclophotocoagulation-plus (ECP-plus), a modified ECP technique that accesses the ciliary body via a pars plana approach rather than a limbal incision. This posterior approach provides direct visualization of the ciliary processes, circumventing media opacities and allowing for precise laser titration to minimize complications.

The IOP was reduced by 58% at 1 month and 62% at 6 months. The IOP remained stable in 87% of patients at 12 months. BCVA remained stable or improved for most patients, and there was a significant reduction in pain.

CEaP offers immediate efficacy, significantly reducing both the need for antiglaucoma medications and eliminating the requirement for acetazolamide. Previous studies have reported IOP reductions of 61% to 66% in refractory glaucoma[7]. Feinstein et al. compared ECP-plus with anterior ECP, demonstrating a higher IOP stabilization rate at two years postoperatively (80% vs. 33,3%, $p < 0,001$) and a greater mean IOP reduction (52% vs. 24%, $p = 0,001$)[8]. In our study, CEaP was combined with endoscopic PRP in the same procedure to treat the underlying ischemia.

At one month postoperatively, the IOP stabilization rate was 86,7%, decreasing to 76% at six months—slightly lower than the rate reported by Cheng et al. [10] However, we observed a 58% IOP reduction at one month and a 62% reduction at six months, with significant statistical relevance ($p < 0,0001$). Despite a high rate of loss to follow-up, 16 patients remained under monitoring at 12 months, with 14 maintaining IOP stabilization (87% success rate) and a sustained 63% IOP reduction. The success rate at six months (76%) compared favorably with the 57% reported by Cheng et al[10]. Postoperative BCVA remained stable or improved in 15 patients, with no statistically significant difference from preoperative values. Furthermore, patients experienced significant and lasting pain relief, emphasizing CEaP's effectiveness in improving quality of life.

Moreover, the procedure was performed under locoregional anaesthesia, minimizing anaesthetic risk for patients who often have multiple and serious comorbidities, unlike other glaucoma surgeries that require general anaesthesia

The management of neovascular glaucoma remains challenging, requiring both the treatment of retinal ischemia and effective control of IOP to prevent optic nerve damage and uncontrolled pain[1]. PRP is a well-established treatment that destroys ischemic retinal tissue, thereby decreasing oxygen demand and suppressing vasoproliferative factors such as VEGF[11]. However, PRP may be challenging to perform in the presence

of media opacities including dense cataracts, intravitreal hemorrhage, or corneal edema, which are frequent complications of neovascular glaucoma. Intravitreal anti-VEGF injections are another option for reducing neovascularization by directly lowering intraocular VEGF levels[12]. However, their effects are transient, necessitating repeated injections for sustained efficacy[13]. IOP-lowering agents, such as topical β -adrenergic antagonists, α -2 agonists, and carbonic anhydrase inhibitors, reduce aqueous production and may enhance uveoscleral outflow[11]. However, medication adherence is often poor; as demonstrated by Olthoff et al., between 5% and 80% of patients fail to comply with treatment regimens, particularly in chronic cases[14]. Nonadherence may be intentional or unintentional, with forgetfulness playing a **major** role[15]. Additionally, prolonged topical therapy is associated with dry eye syndrome, which negatively affects quality of life[16]. Filtering surgeries, including trabeculectomy and glaucoma drainage devices (e.g., Ahmed valve), may be considered. However, the inflammatory environment in neovascular glaucoma contributes to a high failure rate[17]. Furthermore, complications such as hyphema, tube exposure, severe hypotony, and vision loss can occur[18].

The complication rate of CEaP was comparable to previous reports in the literature[7, 10, 19]. There were manageable, with no cases of endophthalmitis or phthisis bulbi. Importantly, CEaP had fewer severe complications than trabeculectomy or Ahmed valve implantation, where

hyphema occurs in 35% of cases (16.7% in our study), and **phthisis** bulbi has been reported[20].

Despite its promising outcomes, CEaP has limitations, including high equipment costs and a steep learning curve for endoscopic proficiency. Although the initial investment in an ECP laser console is substantial, the cost per procedure decreases with repeated use. In a study by Ho et Al. the per procedure cost decreased from £819.43 for the initial 42 cases to £341.50 after 332 procedures. Notably, compared with various MIGS devices, ECP was found to have the second lowest per-procedure cost after the first 100 cases[21]. The mean operative time was 47 minutes (± 20). A marked decrease in operative time has been observed with a mean duration of 31,7 minutes (± 6.3) over the course of the last 10 procedures, demonstrating a reduction in operative time as the surgeon becomes more familiar with the procedure.

Additional limitations of this cohort included the retrospective design, lack of a control group, and variability in postoperative follow-up by referring ophthalmologists. **As lens extraction was an inclusion criterion, all included eyes were pseudophakic; consequently, these results may not be generalizable to phakic patients with neovascular glaucoma.** Additional prospective studies involving larger cohorts and extended follow up are needed to confirm these results.

Conclusions

CEaP appears to be a safe and effective treatment for neovascular glaucoma, offering substantial IOP reduction, pain relief, and a favorable safety profile. Given its ability to simultaneously address both retinal ischemia and IOP elevation, CEaP represents a promising alternative to conventional surgical approaches.

Abbreviations/acronyms

ARC (anterior retinal cryotherapy) CEaP (Combined Endoscope assisted Procedures)

CCT (cyclocryotherapy) ECP (endocyclophotocoagulation) ECP-plus (endoscopic cyclophotocoagulation and pars plana vitrectomy) IOP (intraocular pressure)

PRP (panretinal photocoagulation) TSCPC (transscleral cyclophotocoagulation)

VA (visual acuity) VAS (visual analog scale) VEGF (vascular endothelial growth factor)

Declarations

- a. Ethical approval statement: The study was approved by the Ethics Committee of the French Society of Ophthalmology (IRB 00008855, Société Française d'Ophtalmologie IRB#1).
- b. Informed consent statement: Written informed consents for the use of clinical records were obtained from all participants. The written

consent of the patient whose data was used for the figure and video has been obtained.

- c. **Consent for publication:** Written consent for the use of clinical images and video was obtained from the patient depicted in Figure 1 and Supplemental Digital Content 1.
- d. **Availability of data and materials:** Research data is available but is not being shared because patient consent to share their data in a relevant public data repository has not been obtained.
- e. **Competing interest:** The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article
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- g. **Authors' contributions:** M.I., P.R. and S.G. wrote the main manuscript text. M.D. collected data. L.C. and T.D. prepared figure and tables. All authors reviewed the manuscript.
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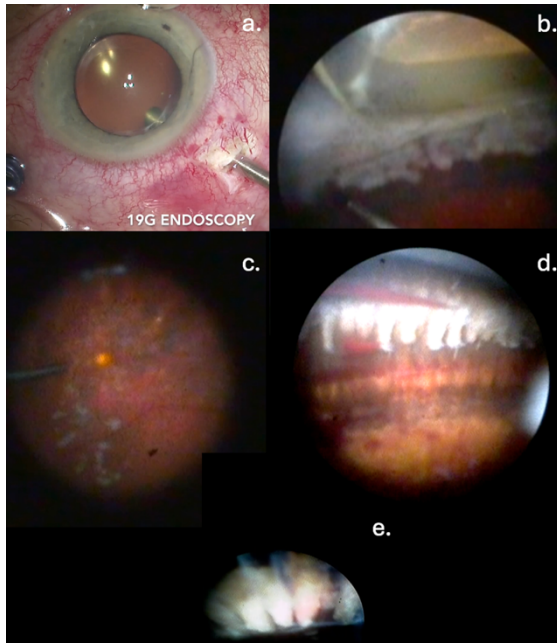


Figure 1: Surgical steps

- 1. Sedation and retrobulbar anesthesia of xylocaine and naropeine*
 - 2. To perform of a sclerotomy 25G at 2 and 8 o'clock*
 - 3. To perform of a sclerotomy 20G at 10 o'clock for the ECP 19G probe (a)*
 - 4. To perform a central and peripheral vitrectomy (b)*
 - 5. Endodiathermy and 360-degree PRP (c)*
 - 6. Visualization of ciliary process (d)*
 - 7. Diode laser cyclophotocoagulation over 270-degree (e)*
 - 8. Visualization of shrinking and whitening of ciliary bodies*
 - 9. Suture of sclerotomies orifice with vicryl rapid 8/0*
 - 10. Subconjunctival of dexamethasone and subtenon injection of naropeine*
- ECP: Endocyclophotocoagulation; PRP: Panretinal photocoagulation*

Characteristic	n=30
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Sex, No. (%)	
Male	19 (63.3%)
Female	11 (36.67%)
Age (yrs, mean $\pm$ standard deviation)	78 ($\pm$ 13,85)
Pseudophakic	30 (100%)
Disease, No. (%)	
PDR	2 (6.67%)
CRVO	18 (60%)
CRAO	5 (16.67%)
BRVO	1 (3.33%)
Melanoma	1 (3.33%)
Unknown	3 (10%)

Table 1: Patients' characteristics

Abbreviations: OVCR: central retinal vein occlusion; CRAO: central retinal artery occlusion; BRVO: branch retinal vein occlusion; PDR: proliferative diabetic retinopathy; Yrs: years

	Preoperative	M1	M6	p-value
IOP value (mmHg, mean $\pm$ standard deviation)	41.77 ($\pm$ 9)	16.2 ($\pm$ 8,1)	15 ($\pm$ 9,35)	
IOP reduction (%)	-	58%	62%	p<0,0001
Success rate** (%)	-	86.7%	76%	
BCVA (logMAR, mean $\pm$ standard deviation) (Snellen visual acuity ratios)	2.26 ($\pm$ 0,753) (HM)		2.37 ($\pm$ 0,699) (HM)	p=0.116

VAS ocular pain* (0-10 scale, mean $\pm$ standard deviation)	3,57 ($\pm$ 2,50)	0,27 ($\pm$ 0,67)	NA	p<0,0001
Hypotensive drops number (mean $\pm$ standard deviation)	2,69	1,67	NA	p=0,00046
Complications	Number (%)			
Hyphema	3 (10%)			
Hyphema + uveitis	2 (6.7%)			
Uveitis	4 (13.3%)			
Corneal oedema	4 (13.3%)			
Hypotony + intravitreal hemorrhage	1 (3.3%)			
Hyphema + hypotony	1 (3.3%)			
Retinal detachment	1 (3.3%)			
Endophthalmitis	0			
Phthisis bulbi	0			
None	14 (46.7%)			

Table 2: Postoperative results

Abbreviations: IOP: Intra-Ocular Pressure; BCVA: Best Corrected Visual Acuity; M1: 1 month; M6: 6 months; VAS: Visual Analog Scale

** Range is 0 (no pain) to 10 (worst pain possible)*

*** Treatment success defined as IOP between 5 and 21 mmHg without additional intervention. At 12 months, 16/30 eyes had available data, of which 14 (87%) met the success criterion; the corresponding IOP reduction was 63% (see Discussion).*