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## Ten years after... are findings of the *Endophthalmitis Vitrectomy Study* still relevant today?

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In 1995, a prospective, randomized study was published on the management of eyes with certain types of acute postoperative endophthalmitis (PE) [3]. Statistical analysis of 420 eyes in the Endophthalmitis Vitrectomy Study (EVS) found benefit neither from systemic antibiotics nor from vitrectomy, unless the visual acuity deteriorated to light perception (LP).

The EVS had a profound worldwide impact. Even in countries without a legal Damocles' sword threatening ophthalmologists who deviate from the EVS recommendations, the study's conclusions regarding no-surgery are closely followed. Vitrectomy became the exception instead of the rule for PE in eyes with >LP vision.

Endophthalmitis satisfies the criterion of an abscess: intracavitary accumulation of purulent material. The volatile mixture, composed of organism, its endo- and exotoxins, cell wall, and several enzymes, as well as various cells/antibodies/humoral agents representing the body's immune response, is bathing that thin, delicate layer of tissue responsible for vision. Even if intravitreal antibiotics successfully destroy the bacteria, the retina may continue to be damaged by the remaining inflammatory debris, and functional recovery is limited by potentially preventable pathologies such as macular edema.

Endophthalmitis is a dynamic event; rather than classifying it as "moderate" or severe," it is much more appropriate to characterize it as "early" or "advanced" [6], reflecting the condition's ability to progress rapidly. It appears rational to *remove*

and remove *all* harmful agents from the vitreous cavity, and to do it *before* visual acuity deteriorates to LP and irreversible damage occurs. As shown in the EVS, foregoing surgery or performing it late increases the phthisis/enucleation risk (6%), delays and limits visual rehabilitation (53% of eyes with  $\geq 20/40$ ), and makes reoperations more common (6% post-treatment vitrectomy rate in the non-surgical group, versus 0% in the surgical group).

Endophthalmitis is one of the most challenging indications for the vitreoretinal surgeon. Visibility is compromised by corneal edema; fibrin, cells, protein, and pus in the anterior chamber; material sticking to the surface of the intraocular lens and lens capsule/s; and by a white and nontransparent vitreous. Additionally, the retina is fragile, often necrotic. To prevent iatrogenic retinal injury and consequent detachment, the EVS protocol prohibited inducing posterior vitreous separation and limited vitreous removal by its "at least 50% of the vitreous" requirement. Such surgery unavoidably leaves purulent material in the *posterior* vitreous. Since patients with PE spend most of their time in bed, the residual pus settles on the retina, explaining the common occurrence of macular hypopyon—a key cause for loss of good macular function in half of eyes in the EVS.

What has changed since the EVS was published, and how can we improve the prognosis of patients with PE?

The strongest argument against "aggressive" surgical intervention is the risk of iatrogenic retinal detachment. However, even the EVS found

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that the rate was 260% higher in the *nonsurgical* than in the vitrectomy group. Furthermore, the infection is much more destructive than a retinal detachment; reattachment surgery can be performed once the infection is cured. Alternatively, silicone oil [1] can be implanted at the conclusion of a complete vitrectomy, after the eye has been irrigated with antibiotics.

Since the early 1990s much has changed in our vitrectomy technology. Current machines offer increased safety in the proximity of the retina due to flow control; probes come in different sizes and with adjustable cutting rates/variable port openings/duty cycle. Visibility is also dramatically improved via panoramic viewing. These improvements now permit intravitreal manipulations such as inducing posterior vitreous detachment or evacuation of macular hypopyon, which would have been too hazardous even a few years ago. We should therefore neither limit vitrectomy to be only core nor accept that “no attempts should be made to excise cortical vitreous” [5].

Our management philosophy focuses on clinical appearance and course, not on visual acuity. While the EVS recommended intravitreal antibiotics as the primary weapon in treating PE, advocating vitrectomy only for eyes with LP vision, we perform vitrectomy unless the endophthalmitis is early *and* there is obvious improvement at 24 h following intravitreal antibiotics injection. If the retina can be visualized or there is good red reflex, we inject intravitreal vancomycin, ceftazidime, and dexamethasone, but we also use topical and oral antibiotics such as ciprofloxacin. We monitor the patient very closely, especially in the first 24 h [6]. This involves detailed consultation with the patient about symptoms such as pain and visual functions to self-monitor, and *hourly* checks by a trained nurse. If the condition does not improve, we offer surgery as an alternative to observation. Most patients, understanding the risks and benefits of surgery versus those of no-surgery, opt for vitrectomy.

Our surgical goal is *complete* vitrectomy, maximal removal of the infectious/inflammatory load from the eye. First, the corneal epithelium is scraped—the temporary keratoprosthesis is used if the corneal stroma is too hazy to permit adequate visualization—then the anterior chamber is cleaned, usually by simple aspiration through a paracentesis. If necessary, the surface of the intraocular lens is also wiped. A large posterior capsulectomy is created to allow irrigation of the bag. Vitrectomy is always three-port; progress is antero-posterior. The typically still attached posterior vitreous cortex is detached and the macular surface carefully vacuumed. Only in the periphery are we rather conservative: the vitreous skirt is shaved to reduce the retinal break risk. This protocol almost always allows complete clearing of the vitreous, yet retinal injury is extremely rare.

In addition to the *method* of treatment, *time* is the other major factor the ophthalmologist can control. Surgery in advanced cases (e.g., LP visual acuity) is more difficult and the prognosis much poorer. The EVS suggested “vitrectomy [to] be undertaken for eyes with the worst clinical appearance at the initial visit”; this approach increases the enucleation/phthisis rate, limits functional recovery potential, and increases the surgical risk.

We cannot directly compare the results of our *complete vitrectomy performed early* philosophy to those of the EVS, although we used identical inclusion/exclusion criteria. In our consecutive series of 47 eyes, 91% achieved  $\geq 20/40$  final visual acuity—as opposed to a 53% rate in the EVS ( $P < 0.0001$ , Fisher’s exact test). No eye developed retinal detachment (nonsurgical group in the EVS: 7%), and only one eye required silicone oil implantation. Enucleation or phthisis has not occurred. There was no case of anatomical failure in our series, as opposed to the EVS with an 11% rate in the nonsurgical group and a 5% rate in the PPP group.

Why is there such a significant outcome difference between our series and the surgery group in the EVS? We believe the improvement is the result of *complete* vitrectomy performed at an *early* stage. We assume that if the EVS protocol had called for such an approach, the study’s results, conclusions, and thus implications would have been similar to ours. The dramatic improvements in surgical technology since the EVS alleviates any criticism of the EVS. Conversely, not to heed the call of time is unacceptable.

The treatment of PE is an evolving process. New antibiotics such as gatifloxacin are introduced, having far superior penetration across the blood-retina barrier [4]. In the 2004 PAT Survey of the American Society of Retina Specialists, 41% of respondents indicated their use of systemic antibiotics “always or at least in selected cases.”

What is then the argument against abandoning the “limit vitrectomy” recommendation of the EVS? It is becoming increasingly difficult to forgo a procedure that improves outcome while actually decreasing the complication rate. Visual rehabilitation is faster and more complete by early and full vitrectomy, and the risk of iatrogenic retinal detachment is reduced as surgical safety increases with panoramic viewing. The consequences of intraoperative retinal tear/detachment development are also less dramatic with silicone oil aiding intraoperative retinal reattachment and maintaining long-term tamponade without risking infection recurrence.

PE is not going to disappear; in fact, its incidence seems to be rising with clear corneal cataract surgery [2]. Evidence is accumulating that the two most important factors in improving prognosis are selecting *clinical appearance and course* to primarily determine therapy, and performing *early complete vitrectomy*. As Celsus stated two millennia ago: “Ubi pus, ibi evacua.” His words could not be truer today.

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