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Microbiologic spectrum and visual outcomes of acute-onset endophthalmitis undergoing therapeutic pars plana vitrectomy

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Abstract

Purpose—To report the clinical presentation, microbiologic spectrum, and visual outcomes associated with acute-onset infectious endophthalmitis undergoing therapeutic pars plana vitrectomy (PPV).

Methods—Multicenter interventional retrospective non-comparative consecutive case series. Billing records were reviewed to identify all charts for patients undergoing PPV within 14 days of diagnosis of acute-onset infectious endophthalmitis over a four-year period at 5 large tertiary referral retina practices. Statistical analysis was performed to assess for factors associated with visual outcomes.

Results—70 patients were identified. The most common clinical setting was post-cataract surgery (n=20). Only three patients (4.3%) presented with 20/400 or better visual acuity (VA). While the majority of patients initially underwent vitreous tap and intravitreal antibiotic injection (n=47, 67.1%), all patients eventually underwent PPV within 14 days of presentation with 68.5% (48/70) of patients undergoing PPV within 48 hours of presentation. Positive intraocular cultures were obtained in 56 patients (80%). The most common identified organism was *Streptococcus* species (n=19). VA at last follow-up was 20/400 or better in 19 patients (27.1%). Three patients underwent evisceration or enucleation (4.3%). Last recorded postoperative VA (mean LogMAR 1.99 +/- 0.94, Snellen VA equivalent finger count) improved from presenting VA (mean LogMAR 2.37 +/- 0.38, Snellen VA hand motions) (P = <0.001). There was no statistically significant correlation between the underlying etiology nor the timing of surgery with this VA outcome.

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Conclusions—Although less than one third of patients achieved 20/400 or better VA, this VA often improved significantly from presenting VA.

Keywords

endophthalmitis; enucleation; evisceration; pars plana vitrectomy; suppurative uveitis

Introduction

Acute-onset infectious endophthalmitis continues to be a significant cause of vision loss, regardless of etiology.[1] Treatment options include diagnostic vitreous tap and injection of antimicrobials or diagnostic and therapeutic pars plana vitrectomy (PPV) with injection of antimicrobials.[2] PPV for endophthalmitis, first described in the 1970s, carries the theoretical advantages of debulking the vitreous cavity of virulent organisms, removing vitreous opacities, and improving intravitreal circulation of antimicrobials.[2-5]

For many years, the optimal patient selection and timing for PPV in the treatment of endophthalmitis was controversial. The Endophthalmitis Vitrectomy Study (EVS), a multicenter prospective randomized controlled trial published in 1995, included 420 eyes with post-cataract surgery endophthalmitis.[6] The EVS demonstrated that for eyes with better than light perception (LP) visual acuity on presentation, outcomes of PPV as initial therapy versus vitreous tap and intravitreal antibiotic injection were the same. Based on these results the EVS recommended that PPV serve as initial therapy for those patients presenting with LP visual acuity or worse.[1,6]

The current applicability of the EVS remains an issue, however, in determining the optimum treatment strategy for the patient with all-cause acute endophthalmitis.

To better understand the present-day outcomes of acute-onset endophthalmitis with PPV, a multicenter retrospective collaborative study was undertaken to analyze the microbiologic spectrum and visual acuity outcomes.

Methods

Institutional review board (IRB) approval was obtained through the individual IRBs at the following institutes for a retrospective consecutive chart review: Wills Eye Hospital, Jefferson Medical College, Philadelphia, Pennsylvania; Associated Retinal Consultants, Oakland University William Beaumont School of Medicine; Bascom Palmer Eye Institute, University of Miami Hospital, Miami, FL; Ophthalmic Consultants of Boston, Boston, MA; New England Eye Center, Tufts University School of Medicine. Research adhered to the tenets of the Declaration of Helsinki and was conducted in accordance with regulations set forth by the Health Insurance Portability and Accountability Act (HIPAA).

Patient records from January 1, 2011 to December 31, 2014 were identified by searching for ICD-9 diagnosis code 361.01 (acute endophthalmitis) and cross-matching for CPT procedure codes 67036 (Pars plana vitrectomy), 66850 (Pars plana lensectomy with fragmatome), 67039 (Pars plana vitrectomy with focal laser) and 67108 (Retinal detachment

repair). Patient records were then reviewed to ensure a clinical description consistent with acute-onset endophthalmitis and all patients with surgical date 14 days or more after the diagnosis of endophthalmitis were excluded.

Clinical and microbiologic records were then reviewed to document the clinical features, microbiologic characteristics, treatment course, and visual acuity (VA) outcomes of each included patient with endophthalmitis. Patients with less than 3 months of follow-up were excluded unless final visual acuity was no light perception (NLP) or the patient underwent evisceration or enucleation.

For statistical analysis Snellen visual acuities were converted to the logarithm of the minimal angle of resolution (LogMAR) scale.[7] For LogMAR values worse than 1.60 the following previously used scale was applied: counting fingers (CF), 2.00; hand motion (HM), 2.30; LP, 2.60; NLP, 2.90.[8,9,10] Paired variables before and after surgery were analyzed using the Wilcoxon signed-rank test. Nonparametric distribution was confirmed using histogram plots. The Kruskal-Wallis test was used to determine if there were differences between multiple groups. All statistical tests were two-tailed and significance was defined as $P < 0.05$. Statistical analysis was performed using Stata version 9.0 (StataCorp, LP, College Station, Texas, USA).

Results

The current study included 70 patients with a mean age of 67.1 years (range 16-97). All cases were unilateral with 40 right eyes and 30 left eyes included. Mean follow-up was 12.5 months (median: 12 months, range 2 weeks to 40 months). Six patients with less than 3 months of follow-up were included: 3 patients had NLP at final visit and 3 patients underwent either enucleation or evisceration.

Baseline Clinical Features and Visual Acuity (Table 1)

The most common clinical settings were post-cataract surgery (n=20), post-intravitreal injection (n=12), and post-trabeculectomy (n=11). Hypopyon was present in 50 of 60 eyes (83.3%) and 69 of 70 eyes (98.6%) presented with no view of the fundus. The majority of patients were pseudophakic with a posterior chamber intraocular lens (43/70, 61.4%). Presenting visual acuities were 20/400 or better (n=3), CF (n=6), HM (n=28), LP (n=30), and NLP (n=3). Of note, the three NLP cases included two cases of acute post-trabeculectomy endophthalmitis that underwent immediate PPV and one case involving an extruding fluocinolone intravitreal implant that necessitated immediate surgical removal simultaneous with PPV.

Treatment Strategies (Table 2)

Initial treatment strategies were vitreous tap and injection of antimicrobials (67.1%, n=47) or PPV with intravitreal antimicrobials (32.9%, n=23). Antimicrobials used included combinations of vancomycin, ceftazidime, gentamicin, amikacin, and voriconazole (in cases of suspected fungal endophthalmitis). Intravitreal corticosteroids were only utilized in 7 patients (10.0%). All patients eventually underwent PPV an average of 2.0 days after initial presentation (range 0 to 14 days). Thirty-five patients (50.0%) underwent PPV within 24

hours of presentation, 13 patients (18.6%) underwent PPV 24 to 48 hours from presentation, and 22 patients (31.4%) underwent PPV between 48 hours and 14 days after presentation. Cannula size used during PPV included 23-gauge (n=48, 68.6%), 25-gauge (n=20, 28.6%), and 20-gauge (n=2, 2.9%).

Microbiologic characteristics (Table 3)

Positive intraocular cultures were obtained in 56 of 70 patients (80.0%). Nearly all positive cultures were obtained from vitreous specimens (n=52) rather than aqueous humor samples (n=4). Vitreous specimens consisted of vitreous tap aspirates from the office (n=29) and PPV specimens (n=23). Patients who went directly for PPV had an undiluted vitreous specimen taken and sent for culture prior to opening an infusion line into the eye. In addition, PPV cassettes were sent for culture at the conclusion of surgery. The most common identified organisms were *Streptococcus* species (n=19) and coagulase-negative staphylococcus (n=14). Of the *Streptococcus* cases 8 occurred following cataract surgery and 4 were associated with infected trabeculectomy blebs. The majority of *Streptococcus* cases were alpha-hemolytic (13/19, 68.4%). Multiple organisms were not present in any culture positive cases. All organisms were sensitive to at least one of the initially administered antibiotics.

Treatment outcomes (Table 4)

VA at last follow-up was 20/400 or better (n=19), CF (n=9), HM (n=14), LP (n=7), and NLP (n=21). Last follow-up post-operative visual acuity (mean LogMAR 1.99 +/- 0.94 (approximately CF), range 0-2.9) improved from presenting visual acuity (mean LogMAR 2.37 +/- 0.38 (approximately HM), range 0.5-2.9) (p = <0.001). Of note, all 3 patients who presented with NLP VA remained NLP after PPV (Figure 1). Three eyes ultimately underwent evisceration or enucleation (4.3%).

15 eyes (21.4%) were noted to have a retinal detachment either at the time of initial PPV or on follow-up. Eight eyes underwent more than one PPV and seven eyes received silicone oil tamponade. In this group, last follow-up visual acuity ranged from CF to NLP except for one eye that ultimately underwent silicone oil removal and had final visual acuity of 20/40 with an attached retina.

On subgroup analysis, while the presenting VA for post-intravitreal injection patients was significantly better than the post-trabeculectomy patients (p=0.025), there was no other statistically significant differences between initial, final or change in VA among post-cataract surgery, post-intravitreal injection, and post-trabeculectomy patients. Similarly, there was no statistically significant difference in initial, final, or change in VA between patient groups undergoing PPV within 24 hours of presentation, between 24 and 48 hours of presentation, and more than 48 hours after presentation. There was a statistically significant improvement in VA from presentation and last follow-up visit in the 23-gauge surgery patients (initial: LogMAR 2.33 +/- 0.43 (approximately HM) last: LogMAR 2.00 +/- 0.91 (approximately CF), p=0.001) but not in the 25 gauge surgery patients (initial: LogMAR 2.50 +/- 0.20 (approximately LP), last: LogMAR 2.04 +/- 0.89 (approximately CF), p=0.634).

On subgroup analysis of the 30 patients who presented with LP vision there was a statistically significant improvement in VA from presentation to last visit (initial: LogMAR 2.6 +/- 0 (approximately LP), last: LogMAR 2.11 +/- 1.15 (approximately CF), p=0.027). Nine patients in this group were post-cataract surgery. 19 patients in this group underwent PPV within 24 hours and average time to PPV was 1.4 days. Four patients improved to 20/400 or better and one patient eventually underwent enucleation. There was no significant difference identified in visual acuity outcome between patients who underwent PPV within 24 hours versus PPV after 24 hours (p=0.37), nor between patients who were post-cataract surgery versus other etiologies (p=0.44).

Discussion

The concept of utilizing PPV in acute-onset endophthalmitis dates to the 1970s, when both small human subject case series and experimental animal model studies demonstrated potential value to early PPV.[3-5,11] Olson *et al.* described selecting endophthalmitis cases for PPV with worse initial VA and more virulent organisms on culture.[12] Another small series reported achieving 20/80 or better in all 5 eyes that underwent PPV within 24 hours of presentation.[13] Vitreous biopsy using the vitrectomy cutter was also noted to have the added benefit of a higher likelihood of positive culture result than a vitreous tap with a needle.[14] The EVS was the first large prospective randomized study examining the role of 20-gauge PPV in endophthalmitis, and based on its cohort of post-cataract endophthalmitis cases, recommended that PPV serve as initial therapy in those patients presenting with LP VA or worse.[6]

The current study is different from the EVS in several ways. First, in the current study, concurrent and pre-existing diseases were not used for exclusion, patients presented at variable times, and multiple surgeons made the decision for the use of vitrectomy. In the EVS, a total of 854 patients with clinical evidence of endophthalmitis were screened for eligibility, but only 420 participants met study criteria and agreed to randomization.[6] Reasons for exclusion included history of intraocular surgery other than cataract surgery (7.5%), history of penetrating trauma (1%), history of glaucoma (12%), history of retinal detachment (2%), and best corrected visual acuity 20/100 or worse before the development of cataract (5.4%).[15] Eyes with NLP VA or retinal detachment at presentation were also excluded.

The strict inclusion/exclusion criteria help explain the difference in VA outcomes between the EVS and the current study. In the EVS, 82.1% of the PPV group and 77.7% of the vitreous tap and injection group achieved 20/200 or better VA.[6] In the current study, however, only 19 of 70 patients (27.1%) reached 20/400 or better VA. Other contributing factors to this difference include selection bias of patients with worse clinical appearance for PPV (nearly all the patients in the current study had no view of the fundus on presentation), a higher incidence of more virulent organisms (e.g. *Streptococcus sp.)* in the current study as compared to the EVS, and inclusion of etiologies that have been shown to have worse outcomes than post-cataract endophthalmitis (e.g. post-trabeculectomy).[16,17]

The current study reflects a different spectrum of patients than the EVS, as less than a third of the cases included in this series occurred in the post-cataract setting. There may be a theoretical benefit to PPV in post-intravitreal injection endophthalmitis patients, given both the higher incidence of monocularity due to coexisting pathology in the other eye (e.g. exudative age-related macular degeneration) and the higher incidence of more virulent organisms (such as *Streptococcus sp.).*[18] Despite the theoretical advantages of PPV in this cohort, subgroup analysis found no significant difference in presentation or final VA between the most common etiologies (post-cataract, post-intravitreal injection, and post-trabeculectomy) except that post-intravitreal injection patients presented with better visual acuity when compared to post-trabeculectomy patients. This difference may be due to a combination of baseline poorer acuity in eyes with advanced glaucoma and earlier presentation by patients after intravitreal injection given strict return cautions.

The average time from presentation to PPV in this study was 2.0 days. On subgroup analysis there was no significant difference in VA outcomes between those patients undergoing surgery in the first 24 hours, the next 24 hours, or beyond 48 hours. A confounding factor in the analysis of surgical timing is that often the decision to perform PPV depends in part on corneal edema and other media factors that may impair the surgeon's ability to perform a safe and more complete PPV. One option in cases with poor view precluding biomicroscopic vitrectomy is the use of an endoscope.[19] Zhang *et al.* recently reported a series of 21 patients undergoing endoscopic-assisted immediate PPV for acute post-cataract endophthalmitis.[20] Of note, two of the 21 patients in that series experienced a retinal detachment within 2 weeks of initial surgery, possibly suggesting that endoscopic PPV still has its pitfalls in optimal viewing to ensure that no retinal breaks are inadvertently created and, if iatrogenic breaks occur that they are able to visualized and treated before completion of surgery. Also, in the current study, among patients presenting with LP visual acuity, while there was a significant improvement in visual acuity from presentation to final visit, only 4 of 30 patients achieved 20/400 or better visual acuity. Surgery within 24 hours did not result in significant improvement compared to surgery beyond 24 hours, although this included patients with all-cause endophthalmitis and not solely post-cataract surgery. There were no significant differences seen between patients post-cataract surgery versus other etiologies, although the sample sizes were likely too small to detect subtle differences.

In this series, the overall improvement in VA from presentation to final visit was reproduced on subgroup analysis of the 23-gauge cases but not the 25-gauge cases. Drawing conclusions related to gauge from either the previous or the current study is impossible given the unequal and non-randomized groups, the non-standardization of technique, and the individual surgeon making decision on gauge selection. However, there may be a theoretical advantage to a smaller platform than 20-gauge in safer vitreous gel removal, especially in light of a likely less than optimal view. A previously reported series reported superior VA outcomes and lower complications in those patients undergoing 25-gauge rather than 20-gauge PPV for endophthalmitis, although only 12 of the 70 included cases were 25-gauge.[21]

The majority of culture-positive cases in the EVS were due to gram-positive coagulase-negative *Staphylococcus sp.*.[6] In contrast, the most common organism identified in the current series was *Streptococcus sp*. These are virulent organisms generally associated with

poorer outcomes; Kuriyan *et al.* reported the largest series of culture-positive *Streptococcus* endophthalmitis with 75% of patients having worse than 20/400 final VA and 25% patients undergoing evisceration or enucleation.[17] Despite the preponderance of *Streptococcus* in the current study, only one of the *Streptococcus* positive cases underwent evisceration or enucleation; two patients in the current study with positive cultures for a different organism (*Candida albicans* and *Bacillus sp.,* respectively) underwent evisceration or enucleation. This may argue that while the overall visual outcomes in this study are poor, similar to other endophthalmitis studies, there may be an anatomically protective benefit to PPV that prevents either phthisis or panophthalmitis from developing and reduces the need for enucleation or evisceration.

The major limitation of this study is its retrospective nature, which lends to a selection bias of cases chosen to undergo PPV. While the use of multiple centers offers the advantage of a larger sample size and a broader geographic spread of causative organisms, there was no defined uniformity in surgical technique or surgeon approach to what constituted a therapeutic PPV (e.g. limited core vitrectomy versus complete core vitrectomy). Timing of surgery and intravitreal antibiotic selection were at the discretion of the individual surgeon, and follow-up periods were not standardized. In addition, including multiple causative etiologies that have different typical clinical courses makes it difficult to draw major conclusions from a retrospective consecutive case series. Despite these limitations, there is useful information to be garnered by analyzing cases undergoing PPV and real world outcomes in the modern surgical era.

In conclusion, PPV for acute-onset infectious endophthalmitis was performed most frequently in post-cataract surgery cases and the most common causative organism was *Streptococcus sp.* infection. Although the overall visual outcomes were poor with less than one third of patients achieving 20/400 vision, visual acuity often improved from presentation to last follow-up visit and the rate of globe loss was lower than may be expected given the virulence of organisms.

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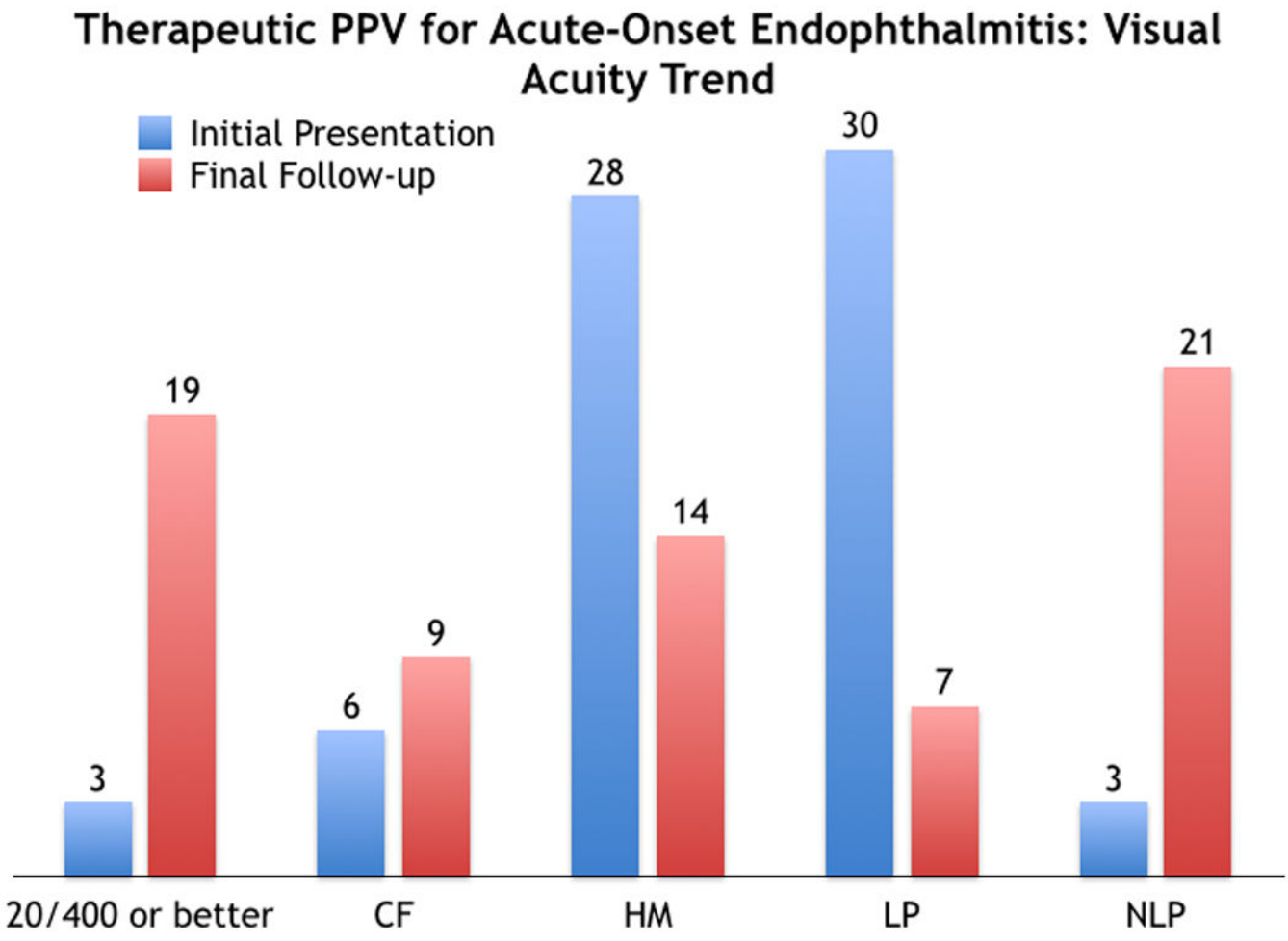

Figure 1.

Therapeutic Pars Plana Vitrectomy for Acute-Onset Endophthalmitis: Visual Acuity Trend from Initial Presentation to Final Follow-up. CF: count fingers; HM: hand motions; LP: light perception; NLP: no light perception

Table 1

Acute Infectious Endophthalmitis Undergoing Therapeutic Pars Plana Vitrectomy: Patient Demographic Characteristics, Causative Etiologies, and Presenting Visual Acuities

	n (% where applicable)
Number of Patients	70
Mean Age	67.1 years (range 16-97)
Hypopyon	60 (83.3%)
Lens Status	
Phakic	19 (27.1%)
PCIOL	43 (61.4%)
ACIOL	2 (2.9%)
Aphakic	6 (8.6%)
Etiology	
CE/IOL	20 (28.6%)
IVI	12 (17.1%)
Trabeculectomy	11 (15.7%)
Trauma	6 (8.6%)
Endogenous	5 (7.1%)
PPV	4 (5.7%)
PKP	3 (4.3%)
Kpro	3 (4.3%)
GDI	2 (2.9%)
Suture removal	1 (1.4%)
DSEK	1 (1.4%)
IV implant removal	1 (1.4%)
Presenting Visual Acuity	
20/400 or better	3 (4.3%)
CF	6 (8.6%)
HM	28 (40.0%)
LP	30 (42.9%)
NLP	3 (4.3%)

ACIOL= anterior chamber intraocular lens; CE/IOL= cataract extraction and intraocular lens placement; CF = count fingers; DSEK= Descemet's stripping endothelial keratoplasty; GDI= glaucoma drainage implant; HM= hand motions; IOL= intraocular lens; IV= intravitreal; IVI= intravitreal injection; Kpro= keratoprosthesis; LP= light perception; NLP= no light perception; PCIOL= posterior chamber intraocular lens; PKP= penetrating keratoplasty; PPV= pars plana vitrectomy

Table 2

Acute Infectious Endophthalmitis Undergoing Therapeutic Pars Plana Vitrectomy: Treatment Strategies

	n (% where applicable)
Number of Patients	70
Initial Treatment Strategy	
T+I	47 (67.1%)
PPV	23 (32.9%)
Mean Time to PPV	2.0 days (range 0-14)
PPV <24 hours	35 (50.0%)
PPV 24-48 hours	13 (18.6%)
PPV >48 hours	22 (31.4%)
PPV Cannula Size	
20-gauge	2 (2.9%)
23-gauge	48 (68.6%)
25-gauge	20 (28.6%)

PPV= pars plana vitrectomy; T+I= vitreous tap and injection; <24 hours= within 24 hours of presentation; 24-48 hours= between 24 and 48 hours of presentation; >48 hours= more than 48 hours after presentation but within 14 days

Table 3

Acute Infectious Endophthalmitis Undergoing Therapeutic Pars Plana Vitrectomy: Microbiologic Spectrum

	n (% where applicable)
Positive Culture Result	56
Vitreous	52 (92.9%)
Aqueous Humor	4 (7.1%)
Gram Positive Bacteria	47 (83.9%)
Streptococcus sp.	19
CNS	14
MRSA	4
Enterococcus sp.	3
Corynebacterium sp.	2
Non-speciated GPC	1
MSSA	1
Bacillus sp.	1
Gemella sp.	1
Peptostreptococcus sp.	1
Gram Negative Bacteria	3 (5.4%)
Moraxella sp.	1
Serratia sp.	1
Pseudomonas sp.	1
Yeast (*Candida sp.*)	4 (7.1%)
Mold	2 (3.6%)
Fusarium sp.	1
Paecilomyces sp.	1

CNS= coagulase-negative *Staphylococcus sp.*; MRSA= methicillin-resistant *Staphylococcus aureus*; MSSA= methicillin-sensitive *Staphylococcus aureus*

Table 4

Acute Infectious Endophthalmitis Undergoing Therapeutic Pars Plana Vitrectomy: Visual Acuity Outcomes

	n (% where applicable)
Number of Patients	70
Final VA	
20/400 or better	19 (27.1%)
20/70 or better	10 (14.3%)
20/70 to 20/400	9 (12.9%)
CF	9 (12.9%)
HM	14 (20.0%)
LP	7 (10.0%)
NLP	21 (30.0%)
Evisc/Enuc	3 (4.3%)

Mean follow-up: 12.5 months. CF= count fingers; Enuc= enucleation; Evisc= evisceration; HM= hand motions; LP= light perception; NLP= no light perception; VA= Snellen visual acuity