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Pars plana vitrectomy for late vitreoretinal sequelae of infectious endophthalmitis: surgical management and outcomes

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Abstract

Purpose—To report the visual acuity (VA) outcomes after pars plana vitrectomy (PPV) for delayed vitreoretinal sequelae of infectious endophthalmitis. All eyes were initially treated with intravitreal antibiotics (Abx).

Methods—Multicenter, retrospective, consecutive case series.

Results—Forty-two eyes met study criteria. The mean follow-up was 48 weeks (SD±61.8). Mean interval from Abx to PPV was 13 weeks (SD±14.3, range 2-70). Indications for PPV included vitreous opacity (VO) (n=22), epiretinal membrane (ERM) (n=9), and retinal detachment (RD) (n=11). LogMAR VA improved from 1.87 (Snellen equivalent: 20/1482) preoperatively to 1.35 (Snellen equivalent: 20/447) at final evaluation ($p<0.001$). logMAR VA improved significantly for patients with vitreous opacities ($P<0.01$) and retinal detachment ($P=0.02$) but not for patients with epiretinal membranes ($P=0.08$).

Conclusions—Patients with infectious endophthalmitis can gain vision if they have a PPV for delayed sequelae such as vitreous opacities or for retinal detachment.

Keywords

Endophthalmitis; epiretinal membrane; pars plana vitrectomy; retinal detachment; surgery; surgical outcomes; uveitis; vitreous opacities

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Introduction

Infectious endophthalmitis remains one of the most devastating ophthalmic diseases and is frequently accompanied by severe vision loss.¹ Loss of visual acuity (VA) is derived from an array of pathological changes, including the more immediate inflammatory and toxic effects, and late structural sequelae, including vitreous opacification, epiretinal membrane, and retinal detachment.²

Late sequelae of endophthalmitis typically have poor visual outcomes.^{2,3} The Endophthalmitis Vitrectomy Study (EVS)⁴, an early large-scale study to examine this cohort, reported that 26.1% of study patients required late procedures, with 7.3% requiring late vitrectomy (defined as >7 days after initial treatment).³ EVS patients requiring late interventions were analyzed in subgroup analysis. Patients who underwent late vitrectomy were included regardless of initial treatment (initially vitrectomy or only a vitreous tap/biopsy). Any patient requiring late surgical interventions had worse VA outcomes, and there was a trend for late interventions to result in modest VA gains.³ Approximately one-third of these late interventions were for three specific indications: vitreous opacities (VO), epiretinal membranes causing macular pucker (ERM), and retinal detachments (RD).³ A more recent publication has supported these indications.²

Since the EVS, infectious endophthalmitis has new medical management and surgical techniques. Newer surgical techniques may result in improved outcomes for patients with these late sequelae. We conducted a multicenter retrospective review examining the visual outcomes of patients undergoing pars plana vitrectomy (PPV) for late sequelae of endophthalmitis.

Methods

We conducted a retrospective, consecutive case series of patients treated at five tertiary eye care centers (Associated Retinal Consultants, William Beaumont Hospital, Oakland University School of Medicine, Royal Oak, MI; Mid Atlantic Retina, Wills Eye Hospital, Jefferson Medical College, Philadelphia, PA; Bascom Palmer Eye Institute, University of Miami Hospital, Miami, FL; Ophthalmic Consultants of Boston, Boston, MA; and, New England Eye Center, Tufts University School of Medicine, Boston, MA). Patient records were identified via diagnosis codes (i.e. “Endophthalmitis”) and surgical billing codes (“PPV”, “PPV with membrane peeling”, “PPV with repair of retinal detachment”, and “PPV with repair of complex retinal detachment”) from 2008 to 2015.

Inclusion/Exclusion Criteria

Inclusion criteria were a diagnosis of infectious endophthalmitis and a PPV greater than 2 weeks (i.e. “delayed PPV”) after initial management. Initial treatment modality (intravitreal antibiotics and/or PPV) did not exclude patients from enrollment in keeping with the EVS protocol.³ Patients included in the current study all underwent vitreoretinal surgery (PPV) for one of three diagnoses: 1) vitreous opacities (VO), 2) ERM, and 3) RD. Exclusion criteria included insufficient follow-up (less than 4 weeks), no light perception (NLP) vision

pre-operatively, and interim intraocular surgery for non-vitreoretinal pathology. Eyes with VO, ERM, or RD prior to development of endophthalmitis were excluded from further analysis.

Patient Management

All patients initially underwent a vitreous tap with intravitreal antibiotics. Surgery was recommended if there was a reasonable chance of surgical success and subsequent structural and/or visual improvement—i.e. the cornea was sufficiently clear to visualize posteriorly, there was no hypotony, and there were no documented sclerotic retinal vessels (or other stigmata of severe macular ischemia). Vitreous opacities were diagnosed by clinical examination and (when necessary) echography, ERM was diagnosed by both clinical examination and optical coherence tomography (OCT), and RD was diagnosed by clinical examination and echography.

Data collection included demographic data, best-corrected visual acuity measurement, and microbiological results from the initial vitreous biopsy. Pre-operative VA was assessed immediately prior to delayed PPV, then post-operative measurements were made serially at all follow-up appointments.

Some patients were diagnosed with multiple vitreoretinal pathologies (for example, both ERM and vitreous opacities). For purposes of statistical analysis, each case was assigned to the one subgroup that would be, theoretically, the most visually significant. Thus, patients with RD were grouped as such, even if ERM and/or vitreous opacities were present. Patients with ERM were grouped as ERM (if no RD present), even if vitreous opacities were present. And, finally, patients with vitreous opacities *only* were analyzed together.

Data analysis

Statistical analysis was performed using Stata version 9.0 (StataCorp, LP, College Station, TX). Snellen BCVA was converted to logMAR units for statistical analyses. Non-parametric comparisons of pre- and post-operative VA were performed utilizing the Wilcoxon Signed Rank Test, and statistical significance was set at $p < 0.05$. The study was approved by the individual Institutional Review Board (IRB)/Ethics Committee at each center, and the study complied with the Health Insurance Portability and Accountability Act of 1996 and adhered to the tenets of the Declaration of Helsinki.

Results

Forty-two eyes of 42 patients met inclusion criteria, with mean follow-up time after vitrectomy of 48 weeks ($SD \pm 61.8$, range 4-256). Demographic data can be found in Table 1. Endophthalmitis was secondary to cataract extraction in 20 patients (47.6%), intravitreal injection in 10 patients (23.8%), and keratoplasty in 6 patients (14.3%). All patients underwent vitreous sampling at the time of intravitreal antibiotic injection. Microbiology results can also be seen in Table 1. No patients underwent repeat intravitreal antibiotic injection. Four patients (9.5%) underwent PPV within 2 weeks after the initial diagnosis of endophthalmitis.

Operative data can be found in Table 2. Mean interval from initial intravitreal antibiotic therapy to PPV was 13 weeks (range 2-70 weeks). At the time of PPV, thirty cases (71.4% of the total cohort) demonstrated vitreous opacities, 10 (23.8%) demonstrated ERM, and an additional 11 (26.2%) demonstrated RD. However, when grouping according to “primary” pathology, twenty-two cases (52.4%) were analyzed as primarily vitreous opacities, 9 (21.4%) as ERM, and an additional 11 (26.2%) as RD.

Detailed VA data for the population, as well as subgroups based on diagnosis, can be found in Table 3. Mean logMAR VA significantly improved from immediately post-initial therapy (2.17 ± 0.9) to the time a decision was made to perform subsequent surgery (1.84 ± 0.12 , $p=0.05$, Wilcoxon Signed Rank test) in the sample of 39 patients who had recorded vision at each time point. Mean logMAR VA prior to delayed PPV and post-intravitreal antibiotics was 1.87 ± 0.77 (Snellen equivalent 20/1482), which improved to 1.35 ± 1.00 (Snellen equivalent 20/447) at final evaluation ($p<0.001$, Wilcoxon Signed Rank test) in 41 patients with recorded vision.

We analyzed subgroups based on the most severe pathology of record. Patients with vitreous opacities had the worst preoperative VA (logMAR VA= 1.95 ± 0.77 ; Snellen equivalent 20/1783) but had the greatest improvement in VA (mean logMAR VA= 1.36 ± 1.00 ; Snellen equivalent 20/458). This difference was statistically significant ($p<0.01$, Wilcoxon Signed Rank test).

Patients with RD likewise demonstrated a statistically significant gain in VA from preoperative VA= 1.89 ± 0.76 (Snellen equivalent 20/1552) to postoperative VA= 1.48 ± 0.95 (Snellen equivalent 20/603; $p=0.02$). Patients with ERM began with preoperative VA of 1.62 ± 0.81 (Snellen equivalent 20/833) and resulted in highest post-operative VA of 1.19 ± 0.76 (Snellen equivalent 20/309). This difference did not reach statistical significance ($p=0.08$).

The time between intravitreal injection and PPV differed between groups. Patients with RD averaged 9.6 weeks (range 4-32). Patients with vitreous opacities averaged 11.9 weeks (range 3-45). Patients with ERM averaged 19.3 weeks (range 4-70).

Additional surgical details were noted: first, for RD cases, only 6 (55%) had a retinal tear identified, of which half had a single defect and half had multiple defects. Silicone oil was utilized for post-operative tamponade in 6 (55%)—gas was used in the remaining 45 percent—and all patients with silicone oil still had oil at final follow-up. Proliferative vitreoretinopathy (PVR) was only observed in 3 cases (27%). Second, recurrence of ERM was only noted in one case after delayed PPV. And, third, recurrence of RD occurred in 2 cases (18%) after primary repair.

A small subgroup of patients ($n=4$) had no light perception (NLP) final visual acuity. All of these patients underwent PPV for vitreous opacities. One patient developed NLP vision by postoperative month 1, one by postoperative month 3, and another by postoperative month 6. The fourth patient developed NLP vision in the affected eye many months after the delayed PPV. Three of these patients had positive cultures for highly virulent organisms (2 with oral

Streptococcus species, 1 with Vancomycin-resistant *Enterococcus* (VRE)). All four patients had light perception (LP) vision prior to the late vitrectomy.

If we exclude patients with NLP visual acuity at final follow-up, there remain significant improvements in the visual acuity results (postoperative logMAR VA 1.21, SD±0.92; Snellen equivalent 20/324; p -value<0.001), with 26.3% of the remaining cohort achieving final VA greater than or equal to 20/40. For the vitreous opacities subgroup, mean final logMAR VA improves to 1.01 (SD±0.95; Snellen equivalent 20/205; p -value<0.001).

Discussion

Endophthalmitis is known to result in vitreoretinal sequelae that contribute to long-term vision loss.¹⁻³ In the EVS cohort, 7.3% of all study patients eventually underwent delayed vitrectomy for vitreoretinal pathology, with an additional 1.8% undergoing a delayed scleral buckling procedure.³ The majority of these vitreoretinal surgeries were for the 3 entities observed in our multicenter review: vitreous opacification, RD, and ERM.

Post-endophthalmitis patients requiring any procedures in EVS after the initial intervention fared poorly compared to those that did not—only 29.9% achieved a final VA greater than or equal to 20/40, versus 65.4% of those requiring no procedures after the initial intervention.³ Understandably, patients with primarily media opacities (i.e. opacified vitreous and capsular opacification) fared better than those with retinal pathologies (RD, macular pucker).³

Since the EVS, surgical techniques have advanced including the introduction of 23-, 25-, and 27-gauge vitrectomy instruments.⁵ Simultaneously, the utilization of intravitreal medications has lead to a rise in endophthalmitis of a new variety. These patients were not evaluated by the EVS.⁶⁻⁷ This study aimed to evaluate the outcomes of delayed vitrectomy for the sequelae of endophthalmitis in the current environment of advancing surgical techniques and technologies.

Overall, we found promising results. Patients in the total cohort had improved vision after vitrectomy (p <0.001). However, the VA results were modest, with a mean final logMAR VA of 1.35 (Snellen equivalent: 20/447), and only 23.8% of patients achieving a final VA of 20/40 (54.8% 20/400).

As expected, patients with vitreous opacities (52.4% of the total cohort) demonstrated the greatest improvement in VA (p <0.01). Interestingly, this group began with the worst preoperative VA. Pre- and postoperative VA measurements improved for patients undergoing vitrectomy for ERM (1.62 and 1.19, respectively) and RD (1.95 and 1.36, respectively), though the results in the ERM subgroup were not statistically significant. We were not surprised to find that patients with RD had the worst final VA.

Preoperative patient selection is important. Risk factors for poor vision outcomes include poor initial visual acuity and microbiological results. Patients should be warned about the potential for poor outcomes due to damage to the eye already caused by the initial infection.

The data underscore the effect of PPV in improving VA in the setting of late vitreoretinal sequelae after endophthalmitis, especially when excluding patients at high risk of poor outcomes. However, overall, patients requiring delayed PPV after endophthalmitis have a poor prognosis and final visual acuity results remain poor, with only about half achieving 20/400 and approximately a quarter achieving 20/40. One possible explanation is that delayed vitreoretinal sequelae serve as a proxy for the virulence of the inciting organism, putting these patients at higher risk for poorer outcomes from the outset.³

The study has limitations. First, the study is retrospective and, thus, subject to selection bias. This study differs from the EVS in both inclusion and exclusion criteria⁴. That said, similar biases are present—for example, surgeons selected patients in whom surgical success was deemed possible. This intrinsically selects for better outcomes, rather than looking at all cases of endophthalmitis. Second, we had a small cohort in spite of multicenter recruitment, and this limits the precision of statistical analyses. Third, the group lacked a standardized protocol (such as that used in the EVS) to select patients or for surgical approach. Thus we cannot provide treatment recommendations, but it does improve generalizability of the results. For example, the group used four different surgical gauges (including 27-gauge) to perform surgery. Finally, the method for assigning each patient to a single group—while necessary for clearer analysis—requires a degree of artificial grouping that covers over the individual complexity of the cases included in this series. As a result, multiple pathologies could be present (up to three) in a single case.

The diversity of the cases in our series can be seen in the more detailed patient data available in Table 4. These cases are marked by highly variable treatment courses, multiple surgical pathologies, diverse pathogens, and variable visual results, to name a few. All of these divergent factors must be acknowledged when trying to extend the results of this study to any individual patient—as mentioned above, each of these factors must be considered when deciding whether or not a patient warrants a delayed vitreoretinal surgery. However, it is noteworthy that, in spite of a relatively small and considerably diverse cohort, statistically significant improvement in visual acuity was noted, however modest, in both the overall cohort and in all subgroups (except ERM, which only trended towards statistical significance).

As such, the current study remains the largest review of surgical outcomes for late sequelae of endophthalmitis since the EVS publications, and underscores a few critical points: in general, patients who experience delayed vitreoretinal pathology after endophthalmitis remain at high risk for poorer visual outcomes. Furthermore, patients with poor preoperative VA who are culture-positive for more highly virulent organisms should be counseled about the potential for severe vision loss despite vitrectomy. Although visual prognosis can be determined to some extent by preoperative vision loss, infection severity, or preoperative pathology (vitreous opacities versus RD, for example), visual results are highly variable. In spite of these modest outcomes, vitrectomy can improve the visual outcome in these cases and should be considered in the setting of appropriate expectations and patient selection.

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Summary

Infectious endophthalmitis can precipitate delayed vitreoretinal complications requiring surgery. Pars plana vitrectomy can improve visual acuity outcomes, especially in eyes with vitreous opacities and retinal detachment.

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Table 1
Demographic and Clinical Characteristics of Patients Undergoing Pars Plana Vitrectomy
for Late Sequelae of Endophthalmitis

Feature	Number (%)
N=42 patients	
Age, years	
Mean (range)	67 (12-98)
Gender	
Male	26 (61.9)
Female	12 (28.6)
Not reported	4 (9.5)
Laterality (eye)	
Right	21 (50)
Left	21 (50)
Etiology	
Post-cataract extraction (CE)	20 (47.6)
Post-intravitreal injection (IVI)	10 (23.8)
Post-keratoplasty (including PKP, DSEK, K-Pro)	6 (14.3)
Bleb-associated	2 (4.8)
Traumatic/ruptured globe	2 (4.8)
Post-pars plana vitrectomy (PPV)	1 (2.4)
Not reported	1 (2.4)
Intravitreal antibiotics (initial therapy)	
Vancomycin + Ceftazidime	34 (81.0)
Vancomycin + Ceftazidime + Dexamethasone	5 (11.9)
Other	3 (7.1)
Microbiology Results	
Gram (+) organism	26 (61.9)
Gram (-) organism	2 (4.8)
Fungus (yeast)	1 (2.4)
No growth	8 (19.0)
Not reported	5 (11.9)

* PKP=penetrating keratoplasty, DSEK=Descemet stripping endothelial keratoplasty, K-Pro=keratoprosthesis, PPV=pars plana vitrectomy

Table 2**Operative Data**

Feature	Number (%)
Surgical Indication	
Epiretinal membrane (ERM)	9 (21.4)
Retinal detachment (RD)	11 (26.2)
Vitreous opacities (VO)	22 (52.4)
Interval (Intravitreal Antibiotics to PPV), weeks	
Mean (range)	13 (2-70)
Surgical Gauge	
20-gauge	1 (2.4)
23-gauge	25 (59.5)
25-gauge	15 (35.7)
27-gauge	1 (2.4)
History of previous vitrectomy	
Yes	4 (9.5)
No	38 (90.5)
Follow-up period, weeks	
Mean (range)	48 (4-256)

*
PPV=pars plana vitrectomy

Table 3
Visual Acuity Outcomes

	Pre-Operative VA, logMAR (SD; Snellen equivalent)	Post-Operative VA, logMAR (SD; Snellen equivalent)	P-value (Wilcoxon Signed Rank Test)
Pathology			
Epiretinal membrane (ERM)	1.62 (± 0.81 ; 20/833)	1.19 (± 0.76 ; 20/309)	0.08
Retinal detachment (RD)	1.89 (± 0.76 ; 20/1552)	1.48 (± 0.95 ; 20/603)	0.02
Vitreous opacities (VO)	1.95 (± 0.77 ; 20/1783)	1.36 (± 1.13 ; 20/458)	<0.01
Total Cohort	1.87 (± 0.77 ; 20/1482)	1.35 (± 1.00 ; 20/447)	< 0.001

* VA=visual acuity, logMAR=log of the minimum angle of resolution, SD=standard deviation

Table 4**Detailed patient characteristics**

Case	Age*	Gender	Pathogen	1° Pathology	Additional Pathology	Pre-Op VA	Final VA
1	24	M	No growth	RD	---	LP	HM
2	68	F	Group B Streptococcus	RD	ERM, VO	CF@2'	CF@5'
3	57	F	<i>S. hominis</i>	ERM	VO	20/200	20/200
4	67	M	No growth	VO	---	20/30	20/25
5	84	M	<i>S. gordonii</i>	ERM	VO	HM	CF@6'
6	12	F	No growth	VO	---	LP	HM
7	77	F	No growth	RD	---	HM	HM
8	64	M	<i>S. epidermidis</i>	VO	---	20/400	20/20
9	59	M	<i>S. epidermidis</i>	VO	---	20/30	20/20
10	80	F	No growth	RD	---	20/200	20/80
11	57	M	No growth	RD	---	20/30	20/20
12	58	M	No growth	ERM	---	20/80	20/30
13	50	F	Group B Streptococcus	VO	---	HM	20/100
14	70	M	<i>S. lugdunensis</i>	ERM	VO	LP	20/150
15	67	M	No growth	VO	---	20/100	20/40
16	87	M	No growth	ERM	---	CF@2'	LP
17	83	F	No growth	ERM	VO	20/100	20/100
18	91	F	Streptococcus spp.	RD	---	LP	LP
19	82	F	Peptostreptococcus spp.	VO	---	HM	CF@1'
20	73	M	VRE	VO	---	LP	NLP
21	83	F	<i>S. oralis</i>	VO	---	LP	LP
22	72	M	<i>S. epidermidis</i>	VO	---	CF@2'	20/150
23	73	M	No data	VO	---	HM	CF@4'
24	71	M	Coagulase-negative Staph	ERM	VO	LP	CF@2'
25	75	M	Coagulase-negative Staph	ERM	VO	CF@3'	20/400
26	70	F	No growth	RD	---	CF@1'	20/100

Case	Age*	Gender	Pathogen	1° Pathology	Additional Pathology	Pre-Op VA	Final VA
27	20	M	<i>S. epidermidis</i>	VO	---	CF@2'	20/80
28	69	M	No data	VO	---	N/r	NLP
29	87	M	<i>S. epidermidis</i>	VO	---	CF@2'	20/25
30	63	M	<i>S. epidermidis</i>	VO	---	HM	CF@2'
31	65	n/r	No growth	VO	---	CF@2'	20/400
32	74	n/r	<i>P. acnes</i>	VO	---	20/400	20/25
33	71	n/r	<i>S. epidermidis</i>	RD	---	CF@2;	20/40
34	64	n/r	No growth	VO	---	HM	20/20
35	67	M	<i>S. aureus</i>	RD	---	HM	HM
36	65	M	<i>S. epidermidis</i>	RD	---	20/400	20/400
37	79	M	Enterococcus spp.	RD	---	HM	HM
38	78	M	Streptococcus spp.	VO	---	LP	NLP
39	76	M	Streptococcus spp.	VO	---	LP	HM
40	76	M	Streptococcus spp.	VO	---	LP	NLP
41	70	M	<i>S. epidermidis</i>	ERM	VO	20/200	20/70
42	35	F	<i>K. kristinae</i>	VO	---	HM	20/200

* At time of delayed vitrectomy; VA=visual acuity, n/r=not recorded, RD=retinal detachment, ERM=epiretinal membrane, VO=vitreous opacities, LP=light perception, CF=counting fingers, HM=hand motions, NLP=no light perception