Review Article



Evaluating the efficacy of pars plana vitrectomy in the management of endophthalmitis after following the endophthalmitis vitrectomy study: A systematic review and meta-analysis

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ABSTRACT

Endophthalmitis is a devastating eye complication that requires prompt and effective treatment. A pivotal study in the field of endophthalmitis treatment is the endophthalmitis vitrectomy study (EVS), conducted over a decade ago. The primary objective of this study was to assess the effectiveness of pars plana vitrectomy (PPV) as a treatment option for endophthalmitis following the EVS study. We conducted a comprehensive search across three databases: PubMed, EBSCO host, and ProQuest. Reference lists of published articles were searched. Our study encompassed research conducted between January 2013 and January 2023 to ensure the most up-to-date findings. The best-corrected visual acuity (BCVA) in logMar, causative agents, and predicting factors for visual outcome were evaluated. Nine studies involving 351 eyes were included in the study; however, only eight were included in the meta-analysis. We observed a significant BCVA improvement compared to baseline at 1 month, >1-3 months, >3-6 months, and ≥ 12 -month follow-up, with mean differences of 1.06 (P < 0.001), 1.25 (P < 0.001), 1.41 (P < 0.001), and 1.01 (P < 0.001), respectively. A causative organism was cultured in 61.4% of cases, and the majority of them were Coagulase-negative Streptococcus, Staphylococcus aureus, and Streptococcus sp. Factor associated with better visual acuity includes a younger age, lower intraocular pressure, and culture-negative endophthalmitis. Meanwhile, culture-positive endophthalmitis particularly Streptococcus sp., lower baseline vision, and presence of retinal detachment at initial presentation were identified as a prognostic for poorer visual outcome. PPV demonstrated a significant visual gain in patients with endophthalmitis in the 1st, 3rd, and 6th months. However, caution is warranted in drawing a definitive conclusion.

KEYWORDS: Endophthalmitis, Pars plana vitrectomy, Postoperative endophthalmitis

Introduction

Indophthalmitis is an intraocular inflammation that may lead to severe visual loss or blindness. Typically endophthalmitis occur after several events such as penetrating trauma, ocular surgeries or injections, or endogenous spread [1]. The primary approach to treating endophthalmitis involves controlling infections, managing inflammation, and providing supportive care. Antibiotics are employed as a conservative treatment to control infections; meanwhile, the vitrectomy approach offers improvement of retinal oxygenation, reduces the inflammatory load and load of infection, offers specimens for diagnostic assessment, reduces disease severity, and accelerates visual rehabilitation [2].

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The pivotal randomized controlled trial (RCT) addressing this matter is the endophthalmitis vitrectomy study (EVS), conducted in the early 1990s. The EVS demonstrated that pars plana vitrectomy (PPV) was beneficial for individuals with light perception (LP) vision at presentation. However, no additional advantages were observed when compared to intravitreal antibiotics alone for cases with hand movements (HM) or better vision [1-3].

It is important to note that in the EVS, PPV was defined as the removal of 50% vitreous using 20 G instrumentation.

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In current practice, micro-incision vitrectomy surgery employs 23 G and 25 G instrumentation for PPV. This technique, often sutureless, contributes to reduced surgical times compared to 20 G surgery. The use of 23 G and 25 G instrumentation not only minimizes intraoperative trauma but also lowers the incidence of complications, including retinal detachment, and diminishes postoperative inflammation and faster postoperative visual recovery. Enhancements in vitrectomy technology, including enhanced visualization facilitated by wide-angle viewing and smaller gauge instruments, could lead to a better visual outcome [1,3,4].

Although the EVS has significantly influenced treatment approaches, new clinical practices have emerged since the study's publication. Furthermore, it is crucial to recognize a notable limitation of the EVS, which exclusively focuses on postcataract surgery endophthalmitis, thus neglecting the exploration of other types of endophthalmitis [5].

Therefore, we aim to evaluate the efficacy of PPV for the treatment of endophthalmitis following the EVS study.

Methods

The systematic review has been officially registered in PROSPERO with the registration number CRD42023463927. Two independent reviewers MA and YS searched three electronic databases: PubMed, Proquest, and Ebsco with the keywords: "endophthalmitis," "postoperative endophthalmitis," "PPV," and "PPV," The search was limited to original studies, English language publications, and a time frame of 10 years to ensure the results remain current. The reference lists of selected articles were examined for additional publication.

Study selection

Full-text articles underwent a comprehensive review for potential inclusion based on the following criteria: (1) randomized controlled trials (RCTs), single-arm trials, cohort studies, case—control studies, case series, and cross-sectional studies were eligible. (2) Inclusion criteria encompassed patients experiencing acute endophthalmitis from any cause within a 6-week timeframe who underwent PPV. (3) The inclusion of best-corrected visual acuity (BCVA) measured in logMar as a continuous variable was required. In cases where multiple treatment arms were present, such as tap and inject and PPV, only studies involving PPV were considered. Studies were excluded if baseline or the outcome VA between tap and inject and PPV could not be distinguished and sample fewer than 20 eyes per treatment group.

Data selection, collection, and extraction

We employed the Mendeley reference manager to manage the identified studies. Initially, a deduplication procedure was done, followed by the evaluation of study titles and abstracts to determine eligibility. This evaluation was conducted independently by two co-authors. If studies were deemed potentially relevant during this preliminary assessment, a comprehensive full-text review was undertaken. In instances of disagreement during the selection or quality assessment phases, these matters were deliberated with two other co-authors to reach a consensus. Relevant data were extracted to perform a qualitative synthesis. The extracted data encompassed details

such as author, year of publication, geographical locations, study designs, and inclusion and exclusion criteria. The primary outcome of this study is baseline, follow-up, and final VA. The secondary outcome was microorganism and prognostic factor of visual acuity (VA).

Quality assessment

The quality of cohort studies will be evaluated using the Newcastle-Ottawa Scale. For the case series studies, we use The Joanna Briggs Institute critical appraisal tool and ROBINS-I for nonrandomized clinical trial study.

Data analysis and synthesis

Our approach will involve qualitative synthesis, integrating data from both the textual content and tables across the included studies. This synthesis is aimed at providing a summary of the characteristics and findings of these studies. We will conduct meta-analyses using the random-effects model. The overall impact will assessed through the analysis of mean difference, along with a 95% confidence interval (CI). For the evaluation of statistical heterogeneity, the I^2 statistic will be employed. The data will be consolidated and computed using the statistical tool Review Manager (RevMan) [Computer program]. Version 5.4. The Cochrane Collaboration, 2020. Oxford, UK.

RESULTS

Study characteristics

A total of 1264 studies were identified through a combination of three databases and manual searching, as illustrated in Figure 1. After a thorough screening process, we included nine studies that investigated the efficacy of PPV and endophthalmitis. These nine studies consist of two nonrandomized controlled trials, two case series, four retrospective cohorts, and one single-arm clinical trial. Eight out of nine studies were included in the meta-analysis, whereas one study was excluded from the meta-analysis due to insufficient data. The participants' age ranged from 32 to 96 years old. Geographically, the distribution involved two studies conducted in the UK, two in the US, two in Iran, and the other three conducted in Australia. Hong Kong, and Germany. Across all studies, there were a cumulative 351 eyes included in the analysis. The cause of endophthalmitis varied: two studies exclusively focused on endophthalmitis due to intravitreal injection (IVI), three studies addressed postcataract endophthalmitis, and the remaining four included various causes of exogenous endophthalmitis such as posttrauma, post-PPV, bleb-related, posttrabeculectomy, and postintraocular lens change. For a comprehensive overview of study characteristics [Table 1].

Visual acuity outcomes

Data were pooled from eight studies, that evaluate the VA outcomes after PPV for endophthalmitis [6-13]. One study was excluded due to insufficient data, despite our attempts to contact the author. Mean changes in BCVA from baseline to specific postoperative intervals: 0−1 month, >1 month−3 months, >3 months−6 months, and ≥12-month post-PPV were examined.

The pooled data revealed a significant improvement in BCVA compared to baseline across various time frames:

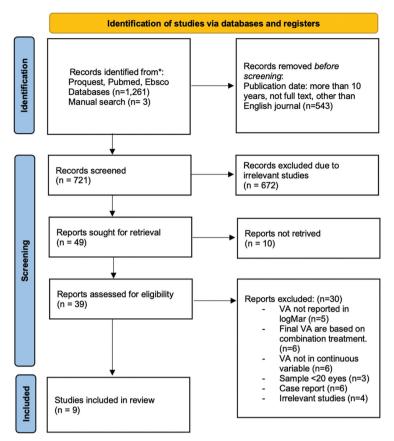


Figure 1: The PRISMA flow for this study

1.06 (95% CI, 0.90–1.21, P < 0.001) for 0–1 month, 1.25 (95% CI, 0.82–1.67, P < 0.001) for >1–3 months, 1.41 (95% CI, 0.82–1.67, P < 0.001) for >3–6 months, and 1.01 (95% CI, 0.86–1.17, P < 0.001) for ≥12 months [Figure 2].

In a subgroup analysis, we found BCVA gains within the first month were notable when PPV was conducted within 24 h 1.09 (95% CI, 0.97–1.21, P < 0.001). Meanwhile, PPV within 1 week also demonstrated a BCVA gain of 1.21 (95% CI, 0.31–2.12, P = 0.009) for 0–1 month, however, it did not reach statistical significance. Notable, over a \geq 12-month follow-up, BCVA improvements persisted for both groups: 1.01 (95% CI, 0.83–1.19, P < 0.001) for PPV within 24 h and 1.04 (95% CI, 0.70–1.38, P < 0.001) for PPV within 1 week [Figure 2].

Meanwhile, in the EVS study, eyes with LP only-VA at presentation had a three times higher chance of reaching 20/40 vision with PPV compared with tap and inject (33% vs. 11%) [3].

Microbiology evaluation

The causative agents of endophthalmitis are shown in Table 2. A causative organism was cultured in 212/345 cases (61.4%) and the majority of them were Coagulase-negative Staphylococcus (79%) followed by Staphylococcus aureus (31.7%) and Streptococcus sp. (16.5%). In the EVS, 69.2% showed positive culture-positive cases, with 46.9% being Coagulase-negative staphylococcus, followed by other Gram-positive cases (15.5%), Gram-negative cases (4.1%), and polymicrobial infections (2.9%).

Factor that influenced the final visual acuity

Factors identified as positive prognostic indicators for final VA outcome include being a younger age (<85 years) [13], intraocular pressure (IOP) \leq 25 mmgHg [13], cataract surgery as the cause of endophthalmitis [12,14], no growth in microbiology [7,8,12,14], having silicon-filled eyes [8], nondiabetic patients [8], and having Gram-positive as the causative agent [12].

On the contrary, adverse prognostic factors for the final VA include a poorer VA at baseline [6,13,14], the presence of retinal detachment at the time of presentation [10,13], undergoing glaucoma surgery compared to IVI or cataract surgery as the cause of endophthalmitis [6], a positive culture for *Streptococcus* sp. compared to coagulase-negative *Staphylococcus* [10,13], and positive microbial culture [13].

Risk of bias

All of the studies have minimal risk of bias [Supplementary Tables 1 and 2, Supplementary Figure 1].

DISCUSSION

In our analysis, the mean changes in BCVA across distinct postoperative intervals revealed a consistent and time-dependent improvement compared to baseline. Specifically, at 0-1 month, >1-3 months, >3-6 months, and ≥ 12 -month post-PPV, with the greatest mean observed at >3-6-month post-PPV (1.41). A sustained improvement was

| Author (year) Country Study design Mean Number PPV Follow-up frequention Treatment Baseline BCVA Inclusion: Guoding Souss eal., UK Case series 76 (13.3) 41 1 (1-3 days) 1 Day (SD) Profusion: Guoding Exclusion: British and inclusion: British and Inclusion: British and Inclusion: Guoding Exclusion: British and Inclusion: British and Inclusion: British and Inclusion: Guoding Exclusion: British and Inclusion: British and Inclusion: British and Inclusion: Guoding Exclusion: British and Inclusion: British and Inclusion: British and Inclusion: Guoding Exclusion: British and Inclusion: British and Inclusion: British and Inclusion: Guoding Exclusion: British and Inclusion: British a | Table 1: Ch | aracterist | Table 1: Characteristics of studies | | | | | | | |
|--|--|--------------|-------------------------------------|--------------|--------|------------------|-------------------|-----------------|---------------|---|
| Australia Retrospective 77.5 (36.2) 64 72 h 12 23 g 3 port PPV 3.1 | Author (year) |) Country | Study design | | Number | - PPV | Follow-up | Treatment | Baseline BCVA | Baseline BCVA Inclusion/exclusion criteria |
| II. UK Case series 76 (13.3) 41 1 (1-3 days) 1 Not mentioned 2.8 (1-2.8) Australia Retrospective cobort study 77.5 (36.2) 64 72 h 12 23 g 3 port PPV 3.1 US Nonrandomized study 81.4 40 3.1 days 6 23 g (63.1%) 22 at A. UK Case series 63 27 Mean 18 23 g (13.4%) 217 (0.37) at A. UK Case series 63 27 Mean 18 23 g (13.4%) 1.66 at A. UK Case series 63 27 Mean 18 23 g (13.4%) 1.66 at A. UK Case series 63 27 Within 6 h 14 23 g (13.4%) 1.66 at I. [9] study 5 Within 6 h 14 23 g (13.4%) 1.66 2 [8] controlled trial 63.8 (11.32) 27 Within 24 h 3 23 g (23.6%) at A. Cobort | | | | age (SD) | eyes | interval | duration (months) | | (Log MAR) | |
| tralia Retrospective 77.5 (36.2) 64 72 h 12 23 g 3 port PPV 3.1 cohort study Nonrandomized 81.4 40 3.1 days 6 23 g (63.1%), 2.2 interventional study Study 20 g (13.4%) 20 g (13.4%) 2.17 (0.37) many Retrospective study 73 (31.11) 30 Within 6 h 14 23 g 2.17 (0.37) Nonrandomized study 64 23 Within 5 h 14 23 g 1.66 Nonrandomized controlled trial 64 23 Within 24 h 3 23 g 2.5 (0.46) single arm 63.8 (11.32) 27 Within 5 h 13.1 Not mentioned 2.1 (0.4-3.0) cohort 20.2 Not mentioned 2.38 (0.19) g Retrospective robort 75.6 (43.0) 17 2 within 24 h 3 23 g 2.1 (0.4-3.0) | Sousa <i>et al.</i> , 2022 [12] | UK | Case series | 76 (13.3) | 41 | 1 (1-3 days) | | Not mentioned | 2.8 (1–2.8) | Inclusion: Acute endophthalmitis and treated with PPV within 7 days, min follow-up of 7 days |
| trafia Retrospective 77.5 (36.2) 64 72 h 12 23 g 3 port PPV 3.1 cohort study Nonrandomized 81.4 40 3.1 days 6 23 g (63.1%), 2.2 interventional study Study Case series 63 27 Mean 18 23 g 2.17 (0.37) interval 7 days Nonrandomized 64 23 Within 6 h 14 23 g 1.66 Study Nonrandomized 64 23 Within 24 h 3 23 g 2.5 (0.46) clinical trial 63.8 (11.32) 27 Within 5 h 13.1 Not mentioned 2.1 (0.4-3.0) cohort Retrospective 75.6 (43.0) 17 2 within 24 h 3 20.2 Not mentioned 2.38 (0.19) ag cohort Retrospective 75.6 (43.0) 17 2 within 24 h 3 cohort Retrospective 75.6 (43.0) 17 2 within 24 h 3 cohort Retrospective 75.6 (43.0) 17 2 within 24 h 3 cohort Retrospective 75.6 (43.0) 17 2 within 24 h 3 cohort Retrospective 75.6 (43.0) 17 2 within 24 h 3 cohort Retrospective 75.6 (43.0) 17 2 within 24 h 3 cohort Retrospective 75.6 (43.0) 17 2 within 24 h 3 cohort | | | | | | | | | | Exclusion: Endogenous endophthalmitis, insufficient outcome |
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| Nonrandomized 81.4 | 2019 [14] | | cohort study | | | | | Tap and inject | | chamber hypopyon and fibrin, loss of red reflex, and vitreous opacities |
| interventional (SD 1.4) 25 g (23.5%), study Case series 63 27 Mean 18 23 g 2.17 (0.37) interval 7 days many Retrospective 73 (31.11) 30 Within 6 h 14 23 g 1.66 study Nonrandomized 64 23 Within 3 h 6 Not mentioned 2.4 controlled trial A Retrospective 76 (10.5) 82 Within 5 h 13.1 Not mentioned 2.1 (0.4–3.0) cohort g Retrospective 75.6 (43.0) 17 2 within 24 h g cohort within 24 h g cohort study No meantioned 2.1 (0.4–3.0) cohort within 24 h | Xu et al., | SO | Nonrandomized | 81.4 | 40 | 3.1 days | 9 | 23 g (63.1%), | 2.2 | Inclusion: Presumptive endophthalmitis after anti-VEGF had occurred |
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| Case series 63 27 Mean 18 23 g 2.17 (0.37) many Retrospective study 73 (31.11) 30 Within 6 h 14 23 g 1.66 Nomrandomized study 64 23 Within 3 h 6 Not mentioned 2.4 controlled trial Single arm 63.8 (11.32) 27 Within 24 h 3 23 g 2.5 (0.46) clinical trial A Retrospective 76 (10.5) 82 Within 5 h 13.1 Not mentioned 2.1 (0.4-3.0) cohort 6 h, 10 6 h, 10 6 h, 10 within 24 h 20.2 Not mentioned 2.38 (0.19) | | | | | | | | | | intraocular or extraocular surgery, endophthalmitis posttrauma |
| Tays | Negretti et al., | , UK | Case series | 63 | 27 | Mean | 18 | 23 g | 2.17 (0.37) | Inclusion: Endophthalmitis cases that failed to improve following |
| Germany Retrospective 73 (31.11) 30 Within 6 h 14 23 g 1.66 study Iran Nonrandomized 64 23 Within 3 h 6 Not mentioned 2.4 controlled trial controlled trial 3 23 g 2.5 (0.46) Iran Single arm 63.8 (11.32) 27 Within 24 h 3 23 g 2.5 (0.46) USA Retrospective 76 (10.5) 82 Within 5 h 13.1 Not mentioned 2.1 (0.4-3.0) Hong Retrospective 75.6 (43.0) 17 2 within 20.2 Not mentioned 2.38 (0.19) Kong cohort cohort 6 h, 10 within 24 h within 24 h | 2020 [11] | | | | | interval | | | | medical therapy or worsening vision despite medical therapy and |
| Germany Retrospective study 73 (31.11) 30 Within 6 h 14 23 g 1.66 Iran Study Nonrandomized (64) 23 Within 3 h 6 Not mentioned 2.4 Iran controlled trial Single arm 63.8 (11.32) 27 Within 24 h 3 23 g 2.5 (0.46) Iran clinical trial USA Retrospective 76 (10.5) 82 Within 5 h 13.1 Not mentioned 2.1 (0.4-3.0) Hong Retrospective cohort 75.6 (43.0) 17 2 within 6 h, 10 6 h, 10 6 h, 10 Kong cohort Within 24 h within 24 h 20.2 Not mentioned 2.38 (0.19) | | | | | | 7 days | | | | proceeded to vitrectomy |
| Fran Nonrandomized 64 23 Within 3 h 6 Not mentioned 2.4 | Januschowski | | , Retrospective | 73 (31.11) | 30 | Within 6 h | 14 | 23 g | 1.66 | Inclusion: Immediate vitrectomy <6 h |
| Iran Nonrandomized 64 23 Within 3 h 6 Not mentioned 2.4 controlled trial controlled trial 3.8 (11.32) 27 Within 24 h 3 23 g 2.5 (0.46) USA Retrospective 76 (10.5) 82 Within 5 h 13.1 Not mentioned 2.1 (0.4–3.0) Hong Retrospective 75.6 (43.0) 17 2 within 20.2 Not mentioned 2.38 (0.19) Kong cohort 6 h, 10 within 24 h within 24 h 20.2 Not mentioned 2.38 (0.19) | et al., 2021 [9] | _ | study | | | | | | | Exclusion: Missing data |
| Controlled trial Single arm 63.8 (11.32) 27 Within 24 h 3 23 g 2.5 (0.46) | Tabatabaei | Iran | Nonrandomized | 64 | 23 | Within 3 h | 9 | Not mentioned | 2.4 | Inclusion: Endophthalmitis due to uncomplicated phacoemulsification |
| Iran Single arm 63.8 (11.32) 27 Within 24 h 3 23 g 2.5 (0.46) USA Retrospective 76 (10.5) 82 Within 5 h 13.1 Not mentioned 2.1 (0.4–3.0) Hong Retrospective 75.6 (43.0) 17 2 within 20.2 Not mentioned 2.38 (0.19) Kong cohort within 24 h within 24 h | et al., 2022 [8] | | controlled trial | | | | | | | with clear cornea incision with HM VA |
| Iran Single arm 63.8 (11.32) 27 Within 24 h 3 23 g 2.5 (0.46) USA Retrospective 76 (10.5) 82 Within 5 h 13.1 Not mentioned 2.1 (0.4–3.0) Hong Retrospective 75.6 (43.0) 17 2 within 20.2 Not mentioned 2.38 (0.19) Kong cohort within 24 h within 24 h within 24 h 13.1 Not mentioned 2.38 (0.19) | | | | | | | | | | Exclusion: Endophthalmitis due to other surgical procedures, history of prior visual loss, history of vitreoretinal surgery, other type of endophthalmitis |
| USA Retrospective 76 (10.5) 82 Within 5 h 13.1 Not mentioned 2.1 (0.4–3.0) cohort Hong Retrospective 75.6 (43.0) 17 2 within 20.2 Not mentioned 2.38 (0.19) (6 h, 10 within 24 h | Najafabadi <i>et al.</i> , 2023 [7] | | _ | 63.8 (11.32) | 27 | Within 24 h | 8 | 23 g | 2.5 (0.46) | Inclusion: Exogenous endophthalmitis |
| Hong Retrospective 75.6 (43.0) 17 2 within 20.2 Not mentioned 2.38 (0.19) Kong cohort 6 h, 10 within 24 h | Weber <i>et al.</i> , 2023 [6] | | Retrospective cohort | 76 (10.5) | 82 | Within 5 h | 13.1 | Not mentioned | 2.1 (0.4–3.0) | 2.1 (0.4–3.0) Inclusion: Exogenous endophthalmitis |
| | Iu <i>et al.</i> , 2023 [10] | Hong Kong | Retrospective cohort | 75.6 (43.0) | 17 | 2 within 6 h, 10 | 20.2 | Not mentioned | 2.38 (0.19) | Inclusion: Acute postoperative endophthalmitis that developed within 6 weeks after cataract operation |
| endophuan | | | | | | within 24 h | | | | Exclusion: Chronic endophthalmitis (later than 6 weeks), combination with other intraocular surgery, other types of endophthalmitis (endogenous, posttraumatic, postintravitreal injection) |

Anti-VEGF: Anti-vascular endothelial growth factor, BCVA: Best-corrected visual acuity, HM VA: Hand movement visual acuity, PPV: Pars plana vitrectomy, SD: Standard deviation, LogMAR: Logarithm of the minimum angle of resolution

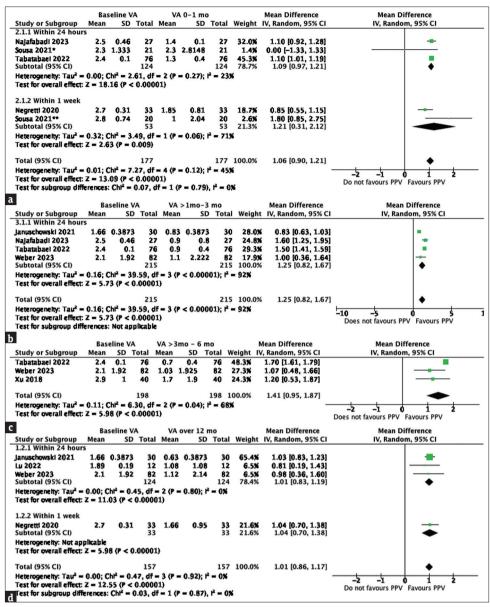


Figure 2: Mean change from baseline best-corrected visual acuity (BCVA) in eyes treated with pars plana vitrectomy. (a) Overall mean BCVA change from baseline to 1 month. (b) Overall mean BCVA change from baseline to >1 months. (c) Overall mean BCVA change from baseline to >3 months-6 months. (d) Overall mean BCVA change from baseline to ≥12 months. CI: Confidence interval, SD: Standard deviation, PPV: Pars plana vitrectomy, VA: Visual acuity

observed even at the extended follow-up of ≥ 12 months (1.01). This may demonstrate a positive impact of PPV on visual outcomes over the long term.

Notably, these BCVA gains within the 1st month were particularly significant when PPV was conducted within 24 h. This might show a potential benefit of early surgical intervention, suggesting a prompt response may contribute to accelerated visual recovery in the initial stages post-PPV. BCVA improvements persist at the ≥12-month follow-up for both subgroups, within 24 h and 1 week.

There remains a debate regarding the optimal timing of PPV. Early PPV, performed within 24 h of presentation, allows prompt removal of infective and inflammatory load in the vitreous, thereby reducing further inflammatory damage to the retina. The EVS mandated immediate vitrectomy within 6 h of presentation, which may not be feasible in clinical settings [15-17]. Meanwhile, another study suggests that the outcomes of early PPV may not be as favorable as an immediate vitreous tap and intravitreal antibiotics injections, followed by a semi-urgent PPV. This is because antibiotics ideally should be administered immediately, before the plateau phase to reduce retinal damage induced by bacterial toxins and inflammatory load. In addition, there is a limited potential for iatrogenic complications possibly associated with early surgery in certain cases [12]. Ultimately, surveys of ophthalmologists have found majority perform early PPV in cases where clinical deterioration within 48 h following tap and inject [15].

| Table 2: Causative | e microor | ganisms i | n endopht | thalmitis | | | | | |
|--------------------------------------|--------------------|-------------------|-------------------|---------------------------------|-----------------------------------|---------------------------|----------------------------|-------------------------|-----------------|
| Study (years) | Number of cases | Culture negative, | Culture positive, | Staphylococcus aureus, n (%) | Coagulase-negative staphylococci, | Enterococcus sp, n (%) | Streptococcus sp, n (%) | Gram-negative, n (%) | Fungi, n (%) |
| | | n (%) | n (%) | | n (%) | | | | |
| Sousa <i>et al.</i> , (2022) [12] | 41 | 16 (39) | 25 (61) | - | 13 (52) | 2 (8) | 6 (24) | 3 (12) | 1 (4) |
| Negretti <i>et al</i> ,. (2020)[11] | 27 | 6 (22) | 21 (78) | 5 (24) | 1 (4.7) | 1 (4.7) | 5 (23.8) | 8 (38) | 1 (4.7) |
| Januschowski <i>et al.</i> , 2021[9] | 29 | 8 (27.5) | 21 (72.5) | 1 (4.7) | 19 (90.5) | - | - | 1 (4.7) | - |
| Tabatabaci <i>et al.</i> , 2022[8] | 23 | 8 (34.8) | 15 (65.2) | 5 (21.7) | 9 (39.1) | - | 1 (4.3) | - | - |
| Najafabadi <i>et al.</i> , 2023[7] | 27 | 9 (33) | 18 (79) | 11 (55.5) | - | - | - | - | - |
| Xu et al., 2018[13] | 40 | 16 (40) | 24 (60) | - | 16 (66.7) | - | 4 (10) | 2 (8.3) | - |
| Iu et al., 2023[10] | 12 | 1 (8.3) | 11 (91.7) | 1 (9) | 3 (27.3) | 3 (27.3) | 2 (18) | 2 (18) | - |
| Ho et al., 2019[14] | 64 | 20 (31) | 42 (66) | 5 (12) | 18 (43) | 2 (5) | 14 (33) | 3 (7) | - |
| Weber <i>et al.</i> , 2023[26] | 82 | 47 (57.3) | 35 (74.4) | 8 (9.8) | 22 (62.8) | - | 3 (8.7) | 2 (5.7) | - |

The EVS demonstrated that PPV was beneficial for individuals with LP vision at presentation with no advantages for cases with HM or better [3]. However, Ho *et al.* observed that patients with baseline VA of LP and HM experienced similar visual improvements, suggesting that early PPV might offer benefits not only for LP vision. Consequently, a clinical trial regarding this area is warranted [14].

The positive culture rate was 61.4% in this study, which was lower than observed in the EVS (69%). Most culture-positive cases in our study are Coagulase-negative *Staphylococcus*, *S. aureus*, and *Streptococcus* sp. as the predominant causative agents. This finding is in line with the EVS results indicating a 70% prevalence of coagulase-negative *Staphylococcus* in cultured-positive cases, which constitute normal flora of human skin [3]. This demonstrated the importance of proper aseptic technique to prevent endophthalmitis postocular surgery or injection. Notably, topical povidone-iodine stands as the sole proven prophylaxis against endophthalmitis, emphasizing the need for its application before using viscous anesthetic agents, which may hinder povidone-iodine's efficacy by forming a barrier [18-21].

The Streptococcus-associated postoperative endophthalmitis rate was 9.0% in EVS [3], with previous studies indicating higher proportions (30.9% and 24.4%) after anti-VEGF injection [20,22]. This suggests a shifting spectrum of organisms between clinical and operating room settings, with Streptococcus species emerging as a more prevalent cause post-IVI. The elevated Streptococcus incidence may be linked to potential aerosol contamination from respiratory flora, highlighting the importance of measures such as restricting patient and provider communication during the procedure to minimize infection risk [20,23,24] or applying povidone-iodine after placement of the lid speculum [25].

Our study demonstrated that culture-positive agents especially *Streptococcal* sp. as the causative agents associated with poorer outcomes, this might be because culture-positive cases may suggest more virulent bacteria and higher intraocular

bacterial load. Studies indicate that *Staphylococcus epidermidis*, as the causative agent of culture-positive endophthalmitis, may be associated with a better visual outcome compared to other pathogens. In addition, Gram-positive organisms, especially *Streptococcal* sp. are linked to worse visual outcomes, possibly due to their virulence causing severe inflammation and tissue damage, limiting chances for improvement even with vitrectomy [26-29].

Our study shows that a lower baseline of VA is a worse prognostic factor. This result was in line with the previous studies, highlighting the association between visual outcomes and initial VA, with poorer VA and retinal detachment predicting unfavorable outcome (odds ratio; 12.2 and 7.7, respectively) [13,26]. In EVS, patients with a presenting IOP >25 mmHg were 1.4 times more likely to experience a decrease in vision compared with those with an IOP between 5 and 25 IOP mmHg [3]. Meanwhile, in Xu *et al.*, the IOP >25 mmHg was 40.8 times (95% CI, 2.1–92.5) less likely to achieve a BCVA of 20/400 or better at the 6-month follow-up compared to those with presenting IOP 5 and 25 mmHg. This possibly reflects increased inflammation or contributing to existing optic neuropathy [13].

This study faces limitations, primarily due to the most of the included studies were case series or retrospective studies, which lowers the overall quality of evidence and makes it susceptible to biases. Furthermore, the research exhibits heterogeneity, due to the inclusion of varied causes of endophthalmitis, including postcataract, IVI, ocular trauma, and others. This variation in etiology may introduce bias, as each source of endophthalmitis could involve different mechanisms, microbial causes, and treatment responses. In addition, our research encountered differences in the selection of PPV treatments, and differences in surgeon skills that may impact surgical outcomes. Furthermore, the difference in durations of follow-up may have an impact on the final vision. From a geographic perspective, while two papers from Iran were included, there was a notable absence of papers

from East and South Asia such as Japan, Korea, and India. This lack of representation from key regions may impact the generalizability of the findings. Considering the findings from both this and earlier studies, it is possible to guide an additional RCT that specifically examines the effectiveness of PPV based on the visual presentation and the cause of endophthalmitis.

Conclusion

PPV demonstrated significant visual improvement in patients with endophthalmitis in the first, third, and 6th months. However, caution is warranted in drawing a definitive conclusion. Additional studies are necessary to establish a comprehensive understanding of this outcome.

Data availability statement

The datasets generated during and/or analyzed during the current study are available in the FigShare repository, entitled PPV for endophthalmitis, DOI 10.6084/m9.figshare.25397257.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Risk of Bias Cohort Studies using Newcastle-Ottawa Scale

| Studies | Selection | Comparability | Outcome | Total |
|----------------------------------|-----------|---------------|---------|-------|
| Ho et al., 2019 [14] | **** | * | *** | 8/9 |
| Januschowski et al., 2021 [9] | **** | * | *** | 8/9 |
| Ho et al., 2023 [10] | **** | * | *** | 8/9 |
| Weber et al., 2023 [6] | **** | * | *** | 8/9 |

^{*1} point, ***3 points, ****4 points

| Supplementary Table 2: Risk of bias case series studies using Joanna Briggs Institute's critical a | appraisal tools | , |
|---|-----------------|------------------|
| JBI checklist questions | Sousa et al., | Negretti et al., |
| | 2022 | 2020 |
| Were there clear criteria for inclusion in the case series? | Yes | Yes |
| Was the condition measured in a standard, reliable way for all participants included in the case series? | Yes | Yes |
| Were valid methods used for the identification of the condition for all participants included in the case series? | Yes | Yes |
| Did the case series have consecutive inclusion of participants? | Yes | Yes |
| Was there clear reporting of the demographics of the participants in the study? | Yes | No |
| Was there clear reporting of clinical information of the participants? | No | No |
| Were the outcomes of follow-up results of cases clearly reported? | Yes | Yes |
| Was there clear reporting of the presenting site(s)/clinic(s) demographic information? | No | No |
| Was statistical analysis appropriate? | Yes | Yes |

| | | | | | Risk of bia | s domains | | | |
|-------|---|--|-------------|-------------|--------------|-----------|----|----|---------|
| | | D1 | D2 | D3 | D4 | D5 | D6 | D7 | Overall |
| Study | Xu 2018 | - | + | - | + | + | + | + | + |
| Str | Tabatabaei 2022 | + | + | - | + | + | + | + | + |
| | | Domains: | due to conf | ounding | | | | Ju | dgement |
| | D2: Bias due to selection of participants. | | | | | | | | |
| | D3: Bias in classification of interventions. D4: Bias due to deviations from intended interventions. | | | | | | | | Low |
| | | D4: Bias due to deviations from intended interventions. D5: Bias due to missing data. | | | | | | | |
| | | D6: Bias i | n measure | ment of ou | | | | | |
| | | D7: Bias i | n selection | of the repo | orted result | | | | |

Supplementary Figure 1: Risk of bias of nonrandomized clinical trial studies with ROBINS-I tool