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REVIEW

Early versus Delayed Vitrectomy for Open Globe Injuries: A Systematic Review and Meta-Analysis

Miguel A Quiroz-Reyes[1], Erick A Quiroz-Gonzalez[2], Miguel A Quiroz-Gonzalez[2], Virgilio Lima-Gómez[3]

[1]Retina Department. Oftalmologia Integral ABC, Affiliated with the Postgraduate Studies Division at the National Autonomous University of Mexico, Mexico City, Mexico; [2]Department of Ophthalmology. Oftalmologia Integral ABC, Affiliated with the Postgraduate Studies Division at the National Autonomous University of Mexico, Mexico City, Mexico; [3]Retina Department. Hospital Juarez de Mexico, Mexico City, Mexico

Correspondence: Miguel A Quiroz-Reyes, The Retina Department of Oftalmologia Integral ABC, affiliated with the Postgraduate Studies Division at the National Autonomous University of Mexico, Mexico City, Mexico, Email drquiroz@prodigy.net.mx

Background: Open globe injuries (OGIs) are a leading cause of monocular blindness worldwide and require prompt intervention to prevent proliferative vitreoretinopathy (PVR) and endophthalmitis when serious intraocular damage occurs. The management of OGIs involves initial wound closure within 24 hours, followed by vitrectomy as a secondary surgery. However, there is a lack of consensus regarding the optimal timing of vitrectomy for maximizing visual outcomes. This meta-analysis aimed to investigate whether early or delayed vitrectomy leads to better outcomes in patients with OGIs.

Methods: This review was conducted based on PRISMA guidelines. The Medline, Embase, Scopus, Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov databases were searched (October 23, 2023). Clinical studies that used vitrectomy to manage OGIs as early (within 7 days) or delayed (8–14 days) interventions were included. Randomized controlled trials (RCTs) and non-RCTs were appraised using the Cochrane risk of bias and JBI tools, respectively.

Results: Eleven studies met the inclusion criteria and were included in the quantitative analyses. There were 235 patients with OGIs who received early intervention and 211 patients who received delayed intervention. The retina was reattached in 91% and 76% of the patients after early and delayed intervention, respectively. Traumatic PVR was present in 9% and 41% of the patients in the early and delayed groups, respectively. The odds of retinal reattachment after vitrectomy were greater in the early group (OR = 3.42, $p = 0.010$, 95% CI=1.34–8.72), and the odds of visual acuity ≥ 5/200 were 2.4 times greater in the early group. The incidence of PVR was significantly greater in the delayed surgery group (OR = 0.16, $p < 0.0001$; 95% CI=0.06–0.39), which also required more than one vitrectomy surgery.

Conclusion: Early vitrectomy results in better postoperative visual acuity, a greater proportion of retinal reattachment, and a decreased incidence of PVR.

Keywords: open globe injury, early vitrectomy, delayed vitrectomy, wound repair, traumatic proliferative vitreoretinopathy, vitrectomy timing

Introduction

Ocular injuries are the leading cause of monocular blindness worldwide. Depending on the type of eye damage, mechanical injury to the globe is categorized as a closed (CGI) or open globe injury (OGI). An OGI is a full-thickness wound of the eye wall caused by a laceration or rupture. Lacerations are usually caused by sharp objects and are subdivided into penetrating injuries, perforating injuries, and intraocular foreign bodies (IOFBs). Penetrating injuries have an entry point but no clear exit point, whereas perforating injuries have both entry and exit points. On the other hand, rupture is caused by considerable blunt force on the globe, leading to rupture of the globe.[1] OGIs have a poorer prognosis than CGIs and can therefore lead to substantial ocular morbidity. Prompt intervention is usually necessary to repair the globe and reduce complications, such as endophthalmitis. The current management suggestion is initial wound closure within 24 hours, followed by secondary surgery, if clinically indicated.[2,3]

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As a secondary surgery, vitrectomy is known to improve the efficacy and prognosis of visual outcomes; however, the optimal timing of vitrectomy remains controversial.[3–5] Ocular trauma may affect several structures within the eye to different extents, making it difficult to plan a unified surgical procedure for all patients. One of the major consequences of OGIs is retinal detachment (RD) complicated by traumatic proliferative vitreoretinopathy (PVR), the incidence of which can be significantly reduced if vitrectomy is performed at the right time, as observed in a retrospective study.[6]

Early vitrectomy performed within a week has been shown to provide better anatomical and visual outcomes than delayed vitrectomy in some studies,[7–9] while other studies have shown better results with delayed vitrectomy performed at 8–14 days.[10] Therefore, there is a lack of consensus on the optimal timing of vitrectomy for severely injured eyes. This systematic review and meta-analysis aimed to systematically review the literature and assess whether early or delayed vitrectomy improves the anatomical and functional outcomes. The primary objective was to investigate the influence of the timing of vitrectomy on anatomical and functional success, which was determined by the rate of retinal reattachment, while functional success was determined by a postoperative visual acuity of 5/200 or better. The secondary objective was to determine the incidence of traumatic PVR and the number of needed pars plana vitrectomy (PPV) procedures.

Methods

The present systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) guidelines.[11] A systematic review protocol was developed, and the patients strictly adhered to the study protocol. A search strategy [see Appendix 1] was used to identify all articles that reported the use of vitrectomy for OGI management.

Study Eligibility Criteria

Studies were selected for inclusion based on the prespecified population, intervention, comparator, and outcome (PICO) framework (Table 1). The aim was to include only randomized controlled trials (RCTs). However, considering the scarcity of RCTs on the topic identified through a preliminary literature search during the protocol writing stage, nonrandomized studies were also included. Conference abstracts, generic reviews, animal studies, and individual case reports were also excluded.

Search Strategy

The following electronic bibliographic databases were searched for clinical trials: MEDLINE, Embase, Scopus, the Cochrane Central Register of Controlled Trials, and Clinical Trials. gov for studies published between 1947 and October 23, 2023. The bibliographies of the included articles were also searched to identify further relevant studies [see Appendix 1].

Data Extraction and Management

Two reviewers (MAQR and EAQG) independently screened titles and abstracts identified in the bibliographic search. Full-text review and data extraction were performed independently, and discrepancies were resolved by mutually comparing the results against the inclusion criteria using Covidence software. The following data were extracted using a standardized platform (Microsoft Excel): first author, year of study publication, study design, mean age and age range of participants, number of eyes included in each group, type of ocular injury, and outcome measures included in the

Table 1 PICO Criteria for the Inclusion of Studies

Parameter	Study selection criteria
Population	People of all ages with OGIs who underwent PPV.
Intervention	Early vitrectomy (within 7 days).
Comparator	Delayed vitrectomy (8–14 days).
Outcomes	Primary outcome (s): Anatomic outcome (retinal reattachment) and functional outcome (postoperative VA ≥ 5/200). Secondary outcome (s): Incidence of traumatic PVR and number of PPV surgeries needed.

Abbreviations: PICO, population, intervention, comparator, outcomes; OGIs, open globe injuries; PPV, pars plana vitrectomy; PVR, proliferative vitreoretinopathy; VA, visual acuity.

individual studies. The data extracted for the meta-analysis included the frequency of retinal reattachment postvitrectomy, the number of eyes that achieved a visual acuity of 5/200 or better, the number of vitrectomies required until the final follow-up visit, and the incidence of traumatic PVR.

Risk of Bias Assessment

The Cochrane Collaboration tool was used to assess the risk of bias (ROB)[12] in the RCTs and prospective cohort studies. These tools incorporate several domains that assess sampling Methods, randomization, reporting bias, and detection bias. The Joanna Briggs Institute (JBI) Critical Appraisal Tool[13] was used to assess ROB in the non-RCTs. The JBI tool has eight domains that assess study details regarding sampling, outcome measurement, analysis, and reporting [see Appendices 2 and Appendices 3]. Two reviewers (MAQR and MAQG) independently assessed the risk of bias in each RCT across the six domains. Disagreements were resolved through consensus.

Measures of Effect of Intervention

The primary outcome measures were the odds of retinal reattachment after vitrectomy (anatomical success) and post-operative visual acuity ≥ 5/200 (functional success). The secondary outcome measure was the incidence of traumatic PVR requiring more than one vitrectomy in either group.

Data Synthesis and Analysis

All outcome measures are expressed as odds ratios (ORs) with corresponding 95% confidence intervals (CIs). A random effects model with the restricted maximum likelihood estimation (REML) approach was used to analyze the data, and forest plots were generated. The existence of statistical heterogeneity between studies was evaluated using I^2 statistics, where values greater than 50% were considered to represent moderate to considerable heterogeneity.[14] A p value < 0.05 was considered to indicate statistical significance. The meta-analysis was performed using R software (version 4.3.1) and the metafor package.[15]

Results

The literature search yielded 2864 articles—2859 through database searches and five through a bibliographic search of the included studies. After removing duplicates, 2260 articles were screened through titles and abstracts, and 40 articles were found to be eligible for a full-text review. Finally, 11 studies met the inclusion criteria and were included in the quantitative synthesis. The PRISMA flowchart for the selection of studies is shown in Figure 1.

The review included 11 studies,[7–10,16–22] one RCT, one prospective cohort study, and nine retrospective observational studies. Among the included studies, six were conducted in the US, three in China and one each in Portugal and Slovenia. This review included 446 patients with OGIs who underwent early vitrectomy within one week (n=235) and delayed vitrectomy between 8–14 days (n=211). The characteristics of the included studies are summarized in Tables 2 and 3.

Visual acuity ≥5/200 was achieved in nearly two-thirds of the patients (97/141) in the early group, while it was achieved in one-half of the patients (55/107) in the delayed group. The retina postvitrectomy was reattached in 91% of the patients (83/91) in the early vitrectomy group and 76% of patients (65/86) in the delayed vitrectomy group. Similarly, traumatic PVR was present in 8 of 90 patients (9%) in the early vitrectomy group, while it was present in 36 of 88 patients (41%) in the delayed vitrectomy group. The percentage of patients who underwent more than one vitrectomy was greater in the delayed group than in the early group (26% [15/57 patients in the early group] vs 40% [24/60 patients in the delayed group]). The Results are summarized in Table 4.

Meta-Analysis

The meta-analysis showed that the odds of retinal reattachment postvitrectomy were significantly greater in the early group than in the delayed group (OR = 3.42, p = 0.010, 95% CI: 1.34–8.72). No heterogeneity was observed in the model fit (Q (df = 4) = 1.9948, I^2=0.00%). A forest plot comparing the efficacy of early versus delayed intervention on retinal reattachment postvitrectomy is presented in Figure 2. Similarly, visual acuity 5/200 or better postvitrectomy was significantly greater in the early group than in the delayed vitrectomy group, with no significant heterogeneity (Q =

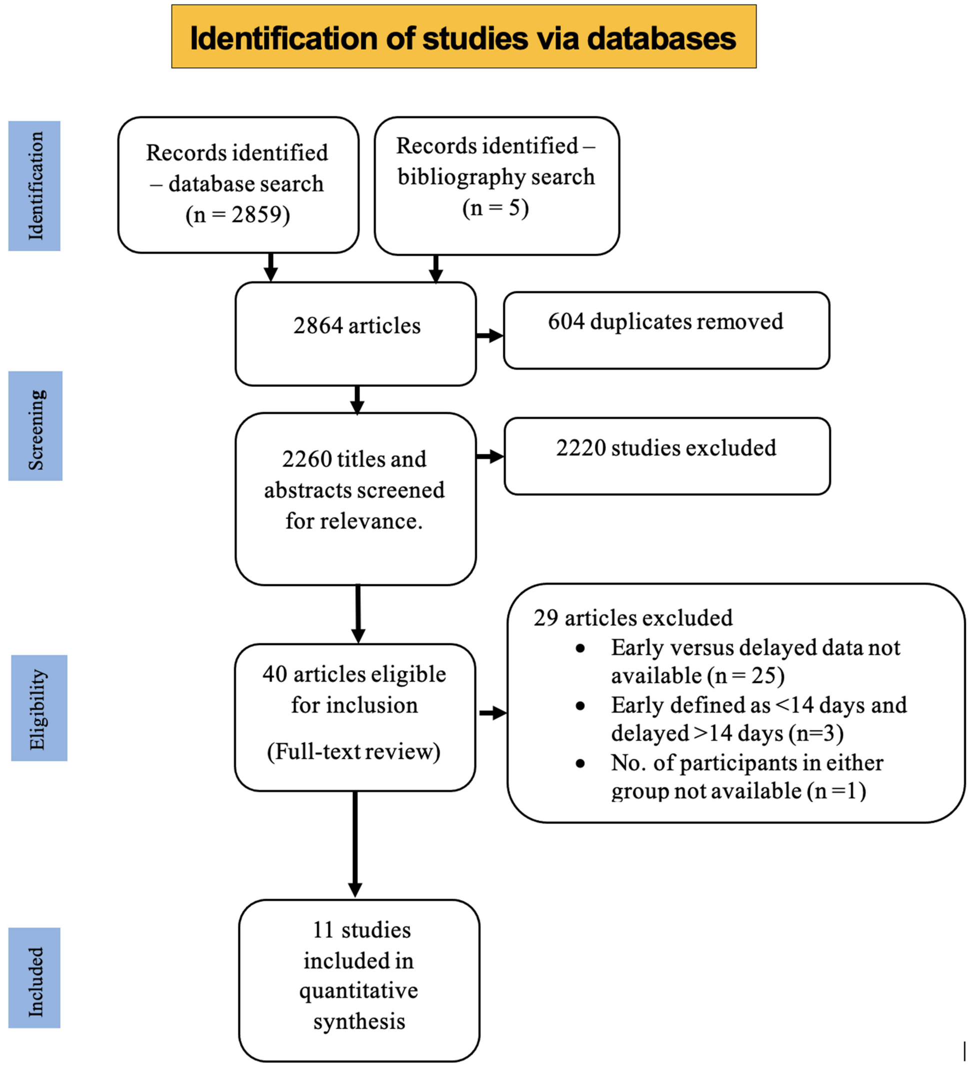

Figure 1 PRISMA flow chart outlining the article selection process.

8.88, df = 6, I^2 = 35.6%). The odds of a visual acuity of 5/200 or better were 2.4 times greater in the early vitrectomy group than in the delayed vitrectomy group (forest plot; Figure 3).

The incidence of PVR was significantly greater in the delayed group (OR = 0.16, $p < 0.0001$, 95% CI: 0.06–0.39). Early vitrectomy resulted in an 84% reduction in the odds of having PVR compared to delayed vitrectomy. Again, there

Table 2 Characteristics of the Included Non Controlled Studies

S.N.	Author/ Year	Country	Study design	Mean age ± SD (age range) years	No. of eyes analyzed early/ delayed group	Type of Injury	Outcome measures
1	Coleman 1982[7]	US	Retrospective observational	NA	37/22	Traumatized open globe injuries	Improvement in VA
2	De Juan et al 1984[8]	US	Retrospective observational	NA	49/54	Penetrating	Visual outcome (Final VA)

(*Continued*)

Table 2 (Continued).

S.N.	Author/ Year	Country	Study design	Mean age ± SD (age range) years	No. of eyes analyzed early/ delayed group	Type of Injury	Outcome measures
3	Ramsay 1985[16]	US	Retrospective observational	5–13	6/4	Double penetrating (Perforating)	Anatomical, functional, and visual outcomes
4	Petrovic et al 2004[22]	Slovenia	Retrospective observational	29.5 (5–67)	29/14	Rupture Penetrating Perforating IOFB	BCVA, RD and PVR at final follow-up
5	Colyer et al 2008[17]	US	Retrospective observational	29 ± 10	3/4	Perforating	Final VA and rates of PVR
6	Ferreira et al 2015[19]	Portugal	Retrospective observational	42 (7–74)	12/6	Perforating	BCVA, rates of global survival and PVR and anatomical success
7	Lin et al 2016[20]	US	Retrospective observational	46.1 (18.3–90.7)	4/4	Rupture IOFB	Visual outcome (BCVA)
8	Yu et al 2019[10]	China	Retrospective observational	36.6±12.8 (10–69)	20/25	Rupture Penetrating Perforating	Functional success, anatomical success, and surgical failure
9	Chauhan et al 2022[21]	US	Retrospective observational	45.2 ± 19.1 (10–92)	39/35	Blunt Sharp IOFB Projectile	Functional and anatomical outcome

Abbreviations: BCVA, best-corrected visual acuity; IOFB, intraocular foreign body; NA, not applicable; PVR, proliferative vitreoretinopathy; RD, retinal detachment; SD, standard deviation; US, United States; VA, visual acuity.

Table 3 Characteristics of the Included Controlled Studies

S.N.	Author/ Year	Country	Study design	Mean age ± SD (age range) years	No. of eyes analyzed early/ delayed group	Type of Injury	Outcome measures
10	Zhang et al 2014[18]	China	Prospective cohort	NA	15/18	Open globe	Retinal reattachment, incidence of PVR, visual recovery and complications
11	He et al 2020[9]	China	Randomized comparative	46.7±11.4 (early group) 42.3±10.3 (delayed group)	21/25	Perforating Rupture	Development of PVR, rates of retinal reattachment, and eye enucleation

Abbreviations: NA, not applicable; PVR, proliferative vitreoretinopathy.

was no heterogeneity associated with this model (Q = 2.58, df = 4, I^2 = 0.00%). The forest plot for the incidence of PVR in early versus delayed vitrectomy patients is presented in Figure 4. More than one vitrectomy had to be performed in more patients who underwent delayed vitrectomy than in those who underwent early vitrectomy.

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Table 4 Summary of the Results from the Included Studies

Study/Year	Outcome Measure	N1	Early (Within 7 Days)	N2	Delayed (8–14 Days)
Zhang et al 2014[18]	PVR development	15	1/15	18	12/18
	Retinal reattachment		14/15		12/18
	BCVA 5/200 or better				
He et al 2020[9]	PVR development	21	3/21	25	10/25
	Retinal reattachment		17/21		15/25
	BCVA 5/200 or better		13		4
	> 1 vitrectomy		3		15
Coleman 1982[7]	PVR development	37		22	
	Retinal reattachment				
	BCVA 5/200 or better		30/37		14/22
De Juan et al 1984[8]	PVR development	43		21	
	Retinal reattachment				
	BCVA 5/200 or better		22/43		9/21
Ramsay et al 1985[16]	PVR development	6		4	
	Retinal reattachment		5/6		1/4
	BCVA 5/200 or better				
Petrovic et al 2004[22]	PVR development	29		14	
	Retinal reattachment		27/29		12/14
	BCVA 5/200 or better				
Colyer et al 2008[17]	PVR development	3	1/3	4	3/4
	Retinal reattachment				
	BCVA 5/200 or better		2/3		2/4
	Final BCVA (mean SD)				
Zhang et al 2014[18]	PVR development	15	1/15	18	12/18
	Retinal reattachment		14/15		12/18
	BCVA 5/200 or better				
Ferreira et al 2015[19]	PVR development	12	1/12	6	1/6
	Retinal reattachment		11/12		4/6
	BCVA 5/200 or better		10/12		4/6
	> 1 vitrectomy		8/12		4/6
Lin et al 2016[20]	PVR development	4		4	
	Retinal reattachment				
	BCVA 5/200 or better		3/4		0/4
	> 1 vitrectomy		2		4

(*Continued*)

Table 4 (Continued).

Study/Year	Outcome Measure	N1	Early (Within 7 Days)	N2	Delayed (8–14 Days)
He et al 2020[9]	PVR development	21	3/21	25	10/25
	Retinal reattachment		17/21		15/25
	BCVA 5/200 or better		13		4
	> 1 vitrectomy		3		15
Yu et al 2019[10]	PVR development	20		25	
	Retinal reattachment		20/20		25/25
	BCVA 5/200 or better		16/20		22/25
	> 1 vitrectomy		2		1
Chauhan et al 2022[21]	PVR development	39	2/39	35	10/35
	Retinal reattachment				
	BCVA 5/200 or better				

Abbreviations: BCVA, best-corrected visual acuity; PVR, proliferative vitreoretinopathy; SD, standard deviation.

Although there was not very high heterogeneity (Q = 6.35, df =3, I^2 = 52.0%) associated with this model, the results did not reach statistical significance (OR = 0.41, p = 0.280, 95% CI: 0.08–2.05) (forest plot; Figure 5).

Risk of Bias Assessment

Of the two controlled studies, the one by Zhang et al (2014)[18] was assessed to have a low risk of bias in five out of seven domains, whereas the one by He et al (2020)[9] was assessed to have an unknown risk of bias across four domains (Figure 6A). Among the noncontrolled studies, six clearly defined their subjects and settings. However, these studies performed poorly when assessed in terms of exposure measurements, criteria used to measure outcomes and controlling for confounding variables (Figure 6B).

Discussion

This systematic review and meta-analysis aimed to determine the influence of vitrectomy timing on OGIs. Previous studies have not provided robust evidence regarding whether early vitrectomy provides effective anatomical and

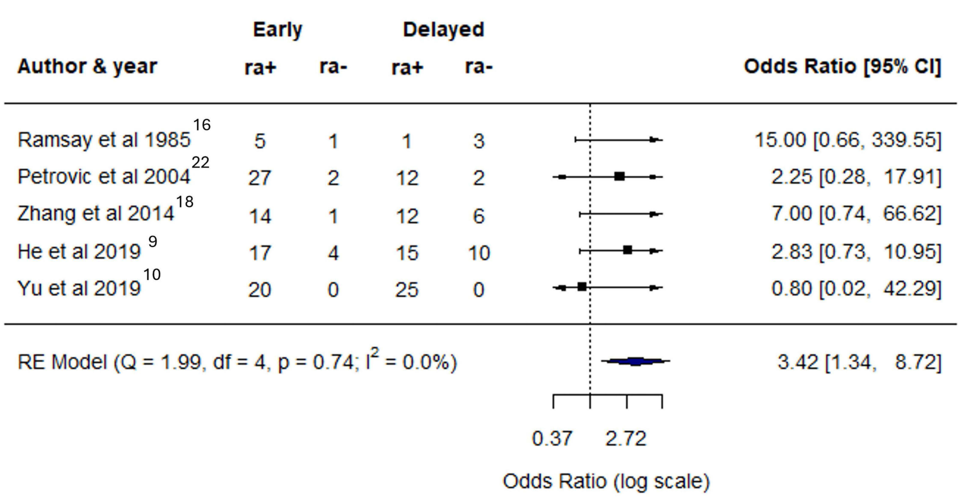

Figure 2 The odds of retinal reattachment postvitrectomy were significantly greater in the early group than in the delayed group; ra+, retina reattached; ra-, retina not attached.

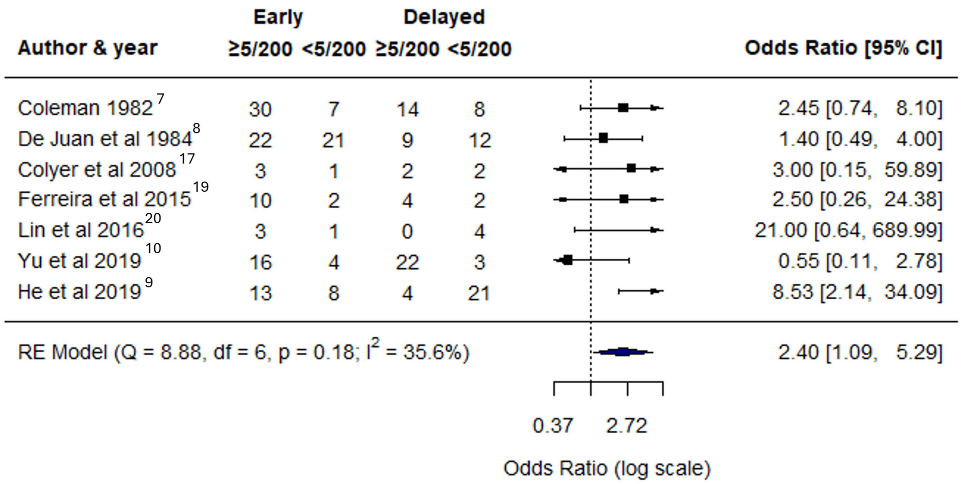

Figure 3 The odds of a visual acuity of 5/200 or better were 2.4x greater in the early group than in the delayed vitrectomy group.

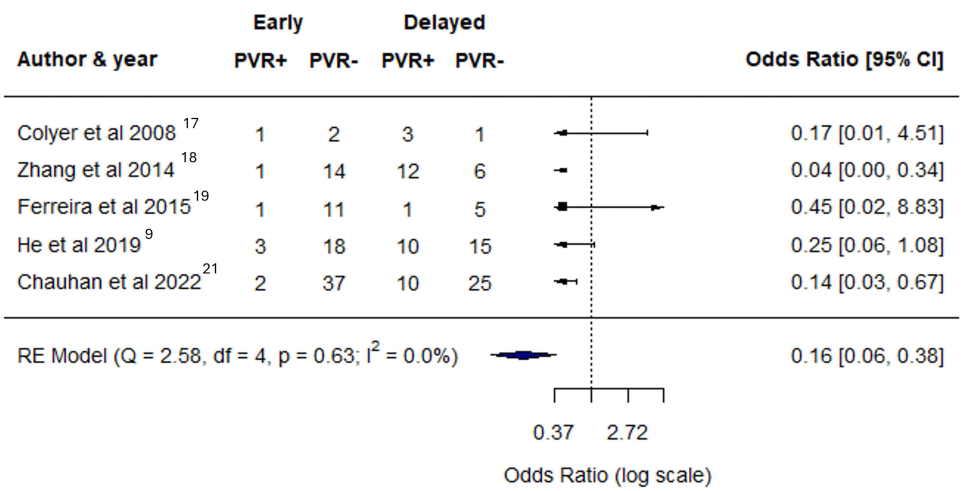

Figure 4 Forest plots comparing the odds of proliferative vitreoretinopathy (PVR) in early and delayed intervention after ocular injury. The incidence of PVR was significantly greater in the delayed group.

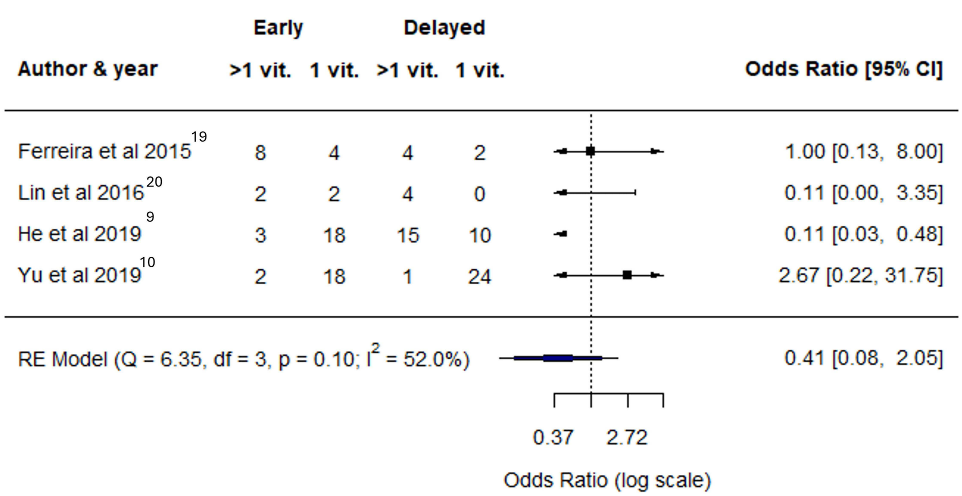

Figure 5 Forest plots comparing the odds of more than one vitrectomy in patients who underwent early or delayed intervention after ocular injury. Patients who underwent delayed vitrectomy were more likely to require more than those who underwent vitrectomy only once.

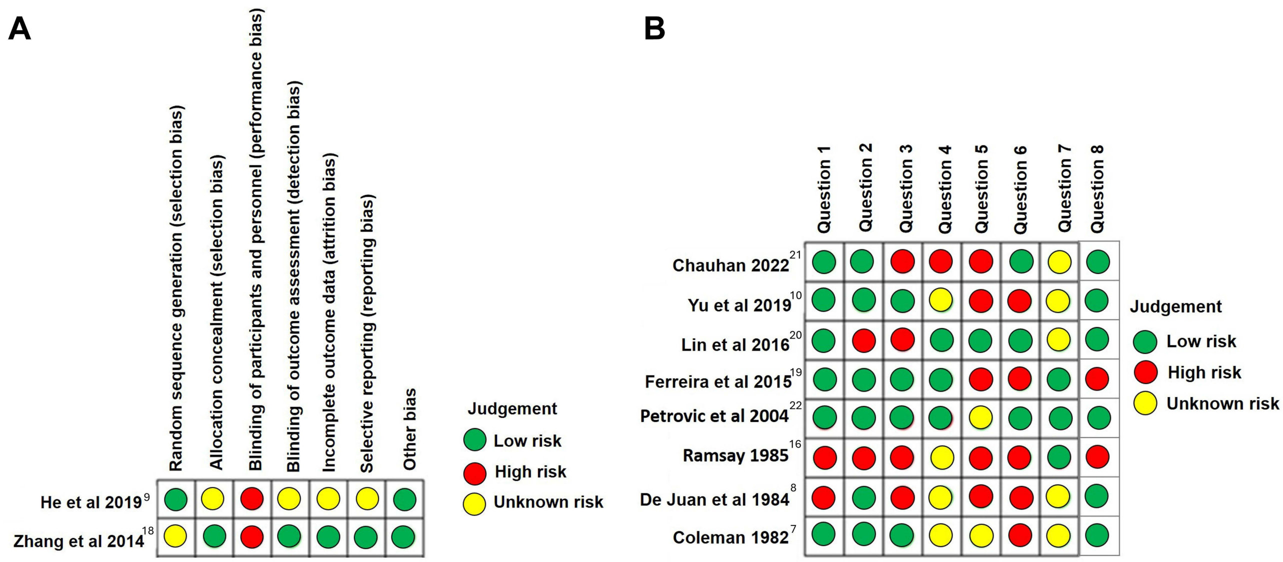

Figure 6 (**A**) Risk of bias assessment of randomized controlled trials. Green indicates a low risk of bias, red indicates a high risk of bias, and yellow indicates an unknown risk of bias. (**B**). Risk of bias assessment of nonrandomized controlled trials. Green indicates a low risk of bias, red indicates a high risk of bias, and yellow indicates an unknown risk of bias.

functional outcomes. There are studies that favor early intervention within 72 hours of injury,[7,8] within 1 week,[9] or delayed vitrectomy within 8–14 days.[10] We systematically reviewed the literature, and the meta-analysis revealed significant findings. The results of our study suggest that early vitrectomy within one week provides significant anatomical outcomes (as evidenced by the odds of occurrence of postoperative retinal reattachment) and functional outcomes (as evidenced by significant postoperative visual acuity $\geq$ 5/200). In particular, we used this cutoff for visual acuity because outcomes better than 5/200 have been described as functional success in the OGI literature.[8,16] Similarly, the frequency of PVR was significantly greater in the delayed vitrectomy group than in the early vitrectomy group. These findings suggest that early vitrectomy within one week results in better anatomical and functional outcomes in the management of OGIs.

The results of our review are consistent with those of earlier studies, namely, Coleman et al (1982)[7] and De Juan et al (1984)[8,] who recommended early vitrectomy, preferably within 72 hours of injury, for better visual recovery. These arguments were made more than four decades ago, and interestingly, there has been a scarcity of well-conducted RCTs in this area, which prompted us to include non-RCTs in the present review. Importantly, our findings also support the findings of only one RCT,[9] in which better anatomical and visual outcomes were observed in patients who underwent vitrectomy within a week. Similarly, there are also reports of vitrectomy performed later than 28 days, where the risk of PVR occurrence was nearly 240-fold greater than that of early vitrectomy.[23] Although we did not investigate the effect of late vitrectomy on PVR development or visual prognosis, our results indicate that the later the vitrectomy is, the worse the prognosis.

However, our findings do not support the use of conventional surgical management for OGIs. In conventional management, also described by Kuhn and Morris as a "mainstream" two-stage approach, wound closure occurs within day 1 of injury, followed by vitrectomy in the second half of the second week.[5] Our results are also inconsistent with a more recent finding that delayed vitrectomy is better than early or late vitrectomy.[10]

The timing of vitrectomy ("when to do it") is an important factor in the management of OGIs.[5] There has been considerable controversy regarding the exact timing of vitrectomy. Early vitrectomy suggests that early intervention helps to prevent the development of fibroblastic tissue within the vitreous cavity, leading to decreased risks of retinal detachment and cyclitic membranes.[5] However, delayed vitrectomy has been preferred by some surgeons because of certain benefits. Mittra and Mieler[4] recommended vitrectomy 7–10 days after injury as a treatment option. Delayed vitrectomy is believed to be less complicated because of the decreased risk of uncontrolled hemorrhage. A delay in vitrectomy also makes the removal of the posterior vitreous easier. However, Ryan and Allen[24] believe that the timing of vitrectomy also depends on other factors, such as the presence of endophthalmitis, retinal detachment, IOFB, severe scleral rupture, and long-standing vitreous hemorrhage.

Assessment of ROB

Controlled studies have demonstrated a high risk of bias for most domains. Surgical interventional studies are likely to be inherently variable because of the nature of the surgery involved. Masking of participants and personnel is difficult because both clinicians and patients are involved in the decision-making process. Noncontrolled studies have shown satisfactory results in terms of subject selection. However, these studies performed poorly in describing the treatment plan and criteria used for outcome assessment. Although noncontrolled studies provide lower levels of evidence owing to an increased risk of bias, they have provided valuable information on the treatment outcome and applicability of treatment strategies, as seen in the present study. Therefore, the value of including these studies in the present review is justified because information that can be assessed from RCTs is unavailable. Noncontrolled studies have provided information and informed potential clinical trials in this area.

This study had several limitations. First, there is a dearth of RCTs available. We found only one RCT, and most of the studies included in the review were uncontrolled. Uncontrolled studies are subject to bias, and unlike RCTs[25] they do not provide a high level of evidence. Second, we were not able to include a few studies in which enough data for meta-analysis were not available because of inadequate reporting.[24,26–31] Third, we studied the effect of early (within 1 week) and delayed (8–14 days) interventions; however, the effects of interventions after 14 days were not present because the search did not provide results available for this review. A network meta-analysis may better explain the effects of interventions with more than two timeframes. Finally, we were unable to assess clinical heterogeneity, which may have affected the outcome. In addition, other factors, such as the preoperative visual acuity, presence of relative afferent papillary defects, zone, location and type of injury, may have affected the outcomes. A subgroup analysis or a meta-regression would have provided more information on the effect of these variables on the outcome measures. However, we did not conduct a subgroup analysis or a meta-regression analysis because of an inadequate number of studies. Despite these limitations, our meta-analysis provided significant results. This review also highlights the paucity of RCTs, and we recommend that additional RCTs in this area are warranted.

Conclusion

Early vitrectomy within 7 days after OGI was associated with better outcomes than delayed vitrectomy between 8–14 days, both of which are approaches after an initial 24-hour globe wound closure. Early vitrectomy leads to better outcomes and is associated with better postoperative visual acuity, greater odds of retinal reattachment, and a decreased incidence of PVR. More RCTs are required to overcome the limitations of this review.

Abbreviations

BCVA, best-corrected visual acuity; CIs, confidence intervals; CGIs, closed globe injuries; IOFBs, intraocular foreign bodies; JBI, Joanna Briggs Institute; NA, not applicable; OGIs, open globe injuries; OR, odds ratio; PICO, population, intervention, comparator, outcomes; PRISMA, preferred reporting items for systematic review and meta-analyses; PVR, proliferative vitreoretinopathy; RCTs, randomized controlled trials; RD, retinal detachment; REML, restricted maximum likelihood; ROB, risk of bias; SD, standard deviation; US, United States; VA, visual acuity.

Data Sharing Statement

The datasets used in this study have been included in the main text. Photographs and figures from this study may be released via a written application to the Photographic Laboratory and Clinical Archives Retina Department at the Oftalmologia Integral ABC Medical and Surgical Assistance Institution (Nonprofit Organization), Av. Paseo de las Palmas 735 suite 303, Lomas de Chapultepec, Mexico City 11000, Mexico and the corresponding author upon request.

Ethics and Consent Statements

This study was conducted at the Retina Department of the Oftalmología Integral ABC. Institution in Mexico City, Mexico. The Institutional Review Board approved the study according to institutional guidelines. No reference numbers have been provided for this systematic review and meta-analysis. This study adhered to the tenets of the Declaration of Helsinki and received full approval from the appropriate research ethics committee, institutional review committee, and institutional teaching department.

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Author Contributions

All the authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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