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The Risk of Sympathetic Ophthalmia Associated with Open-Globe Injury Management Strategies

A Meta-analysis

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Topic: Sympathetic ophthalmia (SO) is a sight-threatening granulomatous panuveitis caused by a sensitizing event. Primary enucleation or primary evisceration, versus primary repair, as a risk management strategy after open-globe injury (OGI) remains controversial.

Clinical Relevance: This systematic review was conducted to report the incidence of SO after primary repair compared with that of after primary enucleation or primary evisceration. This enabled the reporting of an estimated number needed to treat.

Methods: Five journal databases were searched. This review was registered with International Prospective Register of Systematic Reviews (identifier, CRD42021262616). Searches were carried out on June 29, 2021, and were updated on December 10, 2022. Prospective or retrospective studies that reported outcomes (including SO or lack of SO) in a patient population who underwent either primary repair and primary enucleation or primary evisceration were included. A systematic review and meta-analysis were carried out in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines. Random effects modelling was used to estimate pooled SO rates and absolute risk reduction (ARR).

Results: Eight studies reporting SO as an outcome were included in total. The included studies contained 7500 patients and 7635 OGIs. In total, 7620 OGIs met the criteria for inclusion in this analysis; SO developed in 21 patients with OGI. When all included studies were pooled, the estimated SO rate was 0.12% (95% confidence interval [CI], 0.00%−0.25%) after OGI. Of 779 patients who underwent primary enucleation or primary evisceration, no SO cases were reported, resulting in a pooled SO estimate of 0.05% (95% CI, 0.00%−0.21%). For primary repair, the pooled estimate of SO rate was 0.15% (95% CI, 0.00%−0.33%). The ARR using a random effects model was −0.0010 (in favour of eye removal; 95% CI, −0.0031 [in favor of eye removal] to 0.0011 [in favor of primary repair]). Grading of Recommendations, Assessment, Development, and Evaluations analysis highlighted a low certainty of evidence because the included studies were observational, and a risk of bias resulted from missing data.

Discussion: Based on the available data, no evidence exists that primary enucleation or primary evisceration reduce the risk of secondary SO.

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Open-globe injury (OGI) is defined as any injury with a full-thickness wound of the external layers of the eye.[1] It is an ophthalmic emergency and a common cause of preventable unilateral blindness worldwide, especially young patients, with an estimated yearly incidence of 4.49 per 100 000 people in the United States.[2] Management of this sight-threatening condition aims to restore globe integrity, conserve vision, and optimize cosmesis.

A consideration when planning the surgical management of an OGI is the risk of sympathetic ophthalmia (SO). Sympathetic ophthalmia is one of the earliest described ocular pathologic features, with Hippocrates describing a reduction in vision to the fellow eye of an injured eye.[3-5] The term "sympathetic ophthalmia" was coined in 1840 by William McKenzie and was described in histopathologic terms in 1905 by Ernst Fuchs.[6]

Sympathetic ophthalmia is a granulomatous panuveitis incited by the exposure of immune-privileged ocular antigens after trauma or, iatrogenically, after intraocular surgical procedures,[7] with rates reported as 0.01% after vitreoretinal surgery and rising to 0.06% to 0.19% after penetrating trauma.[7,8] Along with a granulomatous panuveitis, Dalen-Fuchs nodules, made up of ephithelioid cells and lymphocytes, also may be found between the retinal pigment epithelium and Bruch's membrane.[6]

Suggested strategies for the modulation of SO risk include removal of the injured eye within 2 weeks of the injury.[9] However, this is controversial, with the risk of SO needing to be balanced against the loss of vision and morbidity associated with eye removal (e.g., psychological impact, quality-of-life issues, phantom eye syndrome).[9] Evisceration and enucleation both are considered as options in risk modification for SO.[10,11] Enucleation and evisceration are proposed to modulate risk through removal of immune-sensitising uveal tissue.[10,11] Enucleation involves the removal of the entire globe and evisceration involves removal of the contents of the globe, preserving the sclera.

In general, the impact of OGI is felt predominantly by younger male people in lower socioeconomic groups.[2] Any clinical advance in the management of patients with this injury and its sequelae will act to reduce the already significant decrease in quality-adjusted life years associated with visual impairment.[12] The clinical need addressed through this meta-analysis reporting the risk of SO secondary to OGI is the optimization of primary surgical management strategies for OGI.

Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[13] A review protocol was registered with the International Prospective Register of Systematic Reviews database (identifier, CRD42021262616).[14] Searches were carried out on June 29, 2021, and were updated on December 11, 2022. The review adhered to the tenets of the Declaration of Helsinki. Because this was a meta-analysis of published studies, institutional review board approval and individual participant consent by the authors of this study was not required.

Three modifications to the registered protocol (edit: October 1, 2021) have been actioned. The first is an arbitrary minimum number of patients in each group (primary repair, primary evisceration, and primary enucleation) was set as 10 patients. Second, inclusion criteria were added in which only studies reporting SO as an outcome in their methodology or results were included. Third, data extraction and bias assessment have been carried out by 3 reviewers, as opposed to 2, as was registered in the original protocol.

Inclusion Criteria

Studies of patients who had sustained an OGI (as defined by Kuhn et al[1]) and reported SO as an outcome in the methodology or results were eligible. Prospective or retrospective studies reporting outcomes including SO in patient populations who underwent either primary repair and primary enucleation or primary evisceration were included. Only articles published in indexed medical journals were included (conference abstracts were excluded). No limitation was placed on language, geographical area of origin, or year of publication. Exclusion criteria were studies that reported < 10 patients who had undergone either primary repair or primary enucleation or primary evisceration and studies that included only patients managed by primary repair or eye removal.

Search Strategy

Five databases: PubMed, CENTRAL, Web of Science, CINAHL, and Embase were searched. Search strings are contained in Annex A (available at www.aaojournal.org).

Risk of Bias Assessment

Three authors independently assessed the potential bias in observational trials using the ROBINS-I tool.[15]

Statistical Methods

The primary outcome was incidence of SO in each primary surgical group. Three independent reviewers each reviewed all titles retrieved from the initial search. Duplicates were eliminated, and, if possible, using abstracts, each reviewer made a decision on its inclusion. If the article could not be included or excluded with certainty on the basis of the abstract, then the full text was read. Any disagreements between reviewers on an article's eligibility were resolved by discussion or, if necessary, arbitration by a senior author (R.J.B.). If a study was reported by > 1 publication, the last publication was used as the reference publication in this review. Included study reference and citation lists were examined for additional studies that may meet inclusion criteria.

The following variables were recorded: study information (first author, publication year, study design, and country of origin), participant information (total number of patients, sex, age range, and median or mean age), sample population information (e.g., study inclusion and exclusion criteria, SO as an outcome [primary or secondary]), intervention information (numbers of in each group of primary repair, enucleation, and evisceration), mean or median follow-up for each group, and injury severity scores recorded as prose.

Descriptive statistics and pooled rates of sympathetic ophthalmia in each group are reported alongside individual study rates. Meta-analysis of pooled rates of SO for each management group was conducted using the meta package in R software version 3.6.1 (R Foundation for Statistical Computing). For studies with no SO cases, 0.05% of the group size was added as the default zero cell value as a method of reducing bias associated with sparse event

data.[16,17] We reported pooled estimates based on a random effects model, although statistical heterogenicity among studies was extremely low, with no notable difference in estimation between fixed and random effects models. Number needed to treat (NNT) was derived from the absolute risk reduction (ARR) as 1 / ARR.

Results

Results of Searches

Eight studies with unique populations met inclusion criteria.[18–25] A Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram of search results is presented in Figure 1. The included studies comprised 7500 patients and 7635 OGIs. In total, 7620 OGIs were eligible for inclusion in this analysis. Where the exact number of primary repairs was not provided in the published articles, the authors of this review assumed that if primary enucleation or primary evisceration did not take place, then primary repair (in the case of Zhang et al,[21] 4796 patients) occurred, because conservative management is not considered a management option for OGIs.[20] In Colyer et al,[18] the primary repair status of 4 eyes was not documented. Two studies, du Toit et al[19] and Bauza et al,[22] included 9 and 1 patients respectively, with OGIs who did not undergo surgical repair. All studies were retrospective observational studies.

Characteristics of Included Studies

Patient characteristics are presented in Table 1. Where recorded (1212 of 7446 patients [16.28%]), 259 patients (21.37%) were female, and 953 patients (78.63%) were male. The mean age ranged from 31 to 44.5 years. Four studies reported injury classification using Birmingham Eye Trauma Terminology notation.[1,20,22–25]

Risk of Bias in Included Studies

An individual risk of bias analysis using the Robins-I tool is presented in Table. 2. The authors allocated a low potential of bias resulting from confounding to each included study because it was believed pragmatically that OGIs undergoing primary enucleation or primary evisceration are likely to have a more severe injury than those undergoing primary repair.[3] All studies were allocated to a low potential risk of selection bias.

Regarding risk of bias in classification of interventions, Zhang et al[21] did not report clearly defined primary repair groups, and the study was allocated to a moderate risk of bias. The risk of bias in all other studies was considered low. Regarding risk of bias in classification of interventions, Zhang et al[21] did not report clearly defined primary repair groups, so potential deviation from intervention is unknown, and a label of "not enough information" was attached. All other studies were judged to have a low risk of bias. Regarding the risk of bias related to missing

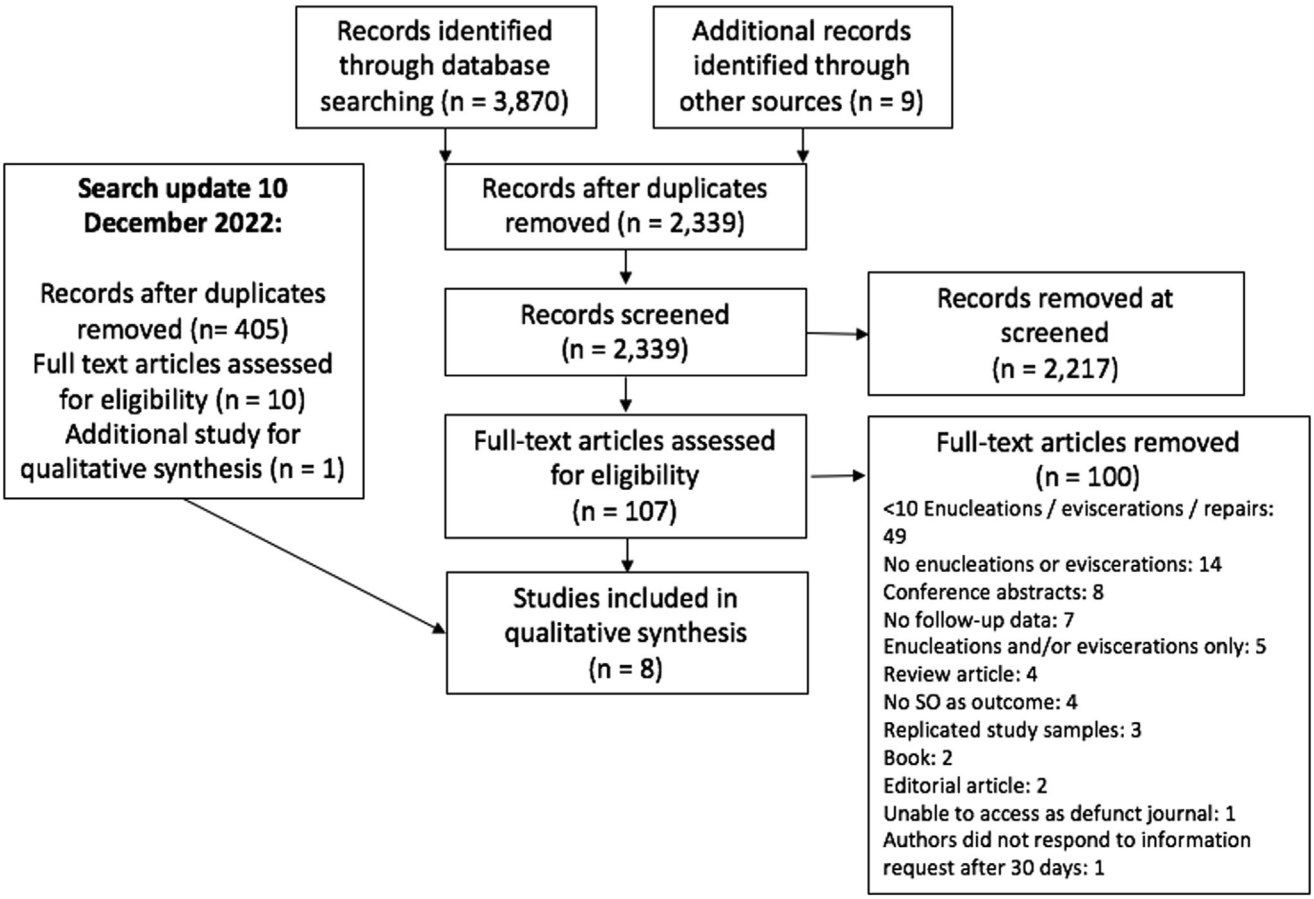

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of study selection. A total of 8 studies were included in the end qualitative synthesis. SO = sympathetic ophthalmia.

Table 1. Characteristics of Included Studies and Patients

Authors (Year)	Country	Male / Female	Age (yrs)	Study Exclusion Criteria	Injury Severity Scoring and Classification	No. of Patients included in This Analysis	No. of Eyes Included in This Analysis	Length of Follow-up	Study Design
Colyer et al (2008)[18]	USA	61 / 0	Mean, 31.0	NA	OTS recorded only for patients who underwent PPV	61	61	Median, 97 days	Retrospective observational
du Toit et al (2008)[19]	Republic of South Africa	NA	NA	NA	NA	1392	1383	> 1 yr, 12.6%; 2 mos—1 yr, 33.0%; 2 wks —2 mos, 22.9%; ≤ 2 wks, 31.5%	Retrospective observational
Savar et al (2009)[20]	USA	523 / 137	Mean, 43.0 in patients who underwent enucleation and 38.0 in those who did not undergo enucleation	Patients who underwent primary surgery at another institution	OTS mean score, 67.15; BETT terminology was recorded for all patients, although not in a mutually exclusive fashion: rupture, 259 (39.0%); laceration, 401 (61.0%); penetrating, 307 (46.6%); perforating, 3 (0.5%); IOFB, 91 (14%)	660	660	Mean, 4.6 mos	Retrospective observational
Zhang et al (2009)[21]	Peoples Republic of China	NA	NA	Patients with systemic autoimmune disease	NA	4843	4968	Range, 2—24 mos	Retrospective observational
Bauza et al (2013)[22]	USA	121 / 27	Mean, 35.9	Self-inflicted OGIs	BETT terminology was recorded for all patients: rupture, 85 (57.4%); laceration, 61 (41.5%); penetrating, 52 (35.1%); perforating, 9 (6.1%); IOFB, 10 (6.8%); mixed (rupture and laceration), 2 (1.4%)	147	148	Mean, 12.45 mos	Retrospective observational

Table 1. (Continued.)

Authors (Year)	Country	Male / Female	Age (yrs)	Study Exclusion Criteria	Injury Severity Scoring and Classification	No. of Patients included in This Analysis	No. of Eyes Included in This Analysis	Length of Follow-up	Study Design
Chang et al (2016)[23]	Republic of China (Taiwan)	134 / 61	Mean, 44.5	Patients with history of prior ocular trauma, patients with a history of ocular conditions affecting VA, and patients with a history of prior intraocular surgery or refractive surgery	194 patients had trauma type recorded: blunt,124 (62.3%); sharp, 70 (35.2%)	195	199	Mean, 13.9 mos	Retrospective observational
Ji et al (2017)[24]	Peoples Republic of China	114 / 34	Mean, 41.5 (male patients) and 50.0 (female patients)	Patients who underwent primary surgery at another institution	All patients had trauma type recorded: rupture, 89 (61.5%); laceration, 59 (38.5%)	148	148	NA	Retrospective observational
Gensheimer et al (2021)[25]	Afghanistan	81 / 3	NA	Patients who did not require surgical intervention	BETT terminology was recorded for 96% of patients (52/54): rupture, 17 (31%); penetrating, 2 (4%); IOFB, 10 (19%); perforating, 3 (6%); mixed, 20 (37%)	54	54	Of the open globe repairs, 60% were followed up > 30 days; this rate was 63% for primary eye removal	Retrospective observational

BETT = Birmingham Eye Trauma Terminology[1]; IOFB = intraocular foreign body; NA = not available; OGI = open-globe injury; OTS = ocular trauma score[26]; PPV = pars plana vitrectomy; VA = visual acuity.

Table 2. ROBINS-I Assessment of Potential Sources of Bias

Source of potential bias	Colyer et al (2008)[18]	du Toit et al (2008)[19]	Savar et al (2009)[20]	Zhang et al (2009)[21]	Bauza et al (2013)[22]	Chan et al (2016)[23]	Ji et al (2017)[24]	Gensheimer et al (2021)[25]
Risk of bias because of confounding	Low	Low	Low	Low	Low	Low	Low	Low
Bias in selection of participants into study	Low	Low	Low	Low	Low	Low	Low	Low
Bias in classification of interventions	Low	Low	Low	Moderate	Low	Low	Low	Low
Bias resulting from deviations from intended interventions	Low	Low	Low	NI	Low	Low	Low	Low
Bias resulting from missing data	Low	Low	Low	Moderate	Low	Low	Low	Low
Bias in measurement of outcomes*	Low	Moderate	Low	NI	Low	Low	NI	Moderate
Bias in selection of the reported result	Moderate	Low	Low	Low	Low	Low	Low	Low
Overall bias judgement	Low	Low	Low	Moderate	Low	Low	Low	Low

NI = not enough information.

data, Zhang et al[21] did not report clearly defined primary repair groups, so group-specific data are unknown. All other studies were assessed as having a low risk of bias.

Regarding the risk of bias relating to measurement of outcomes, du Toit et al[19] reported that 31.5% of patients completed 2 weeks follow-up or less, and Colyer et al[18] reported a median follow-up of 97 days. Becuase 80% of patients with SO demonstrate symptoms within 3 months, it was believed that a moderate risk of bias was appropriate for these studies.[4] Zhang et al[21] did not report clearly defined intervention groups and, therefore, outcome groups, and Ji et al[24] did not report the length of follow-up. All other studies were considered to have a low risk of bias.[22] Gensheimer et al[25] reported in their limitations section that loss to follow-up among Afghan military members or civilians may limit the validity of their follow-up data. All studies were allocated a low risk of bias in selection of the overall reported results.

Findings

Eight studies included SO as an outcome.[18–25] Two studies reported cases of SO: Savar et al[20] reported 3 cases in patients who had undergone primary repair (0.462%); Zhang et al[21] reported 18

Table 3. Primary Surgical Procedures Carried out and Sympathetic Ophthalmia Cases

Authors (Year)	No. of Primary Repairs	No. of Primary Enucleations	No. of Primary Evisceration	Sympathetic Ophthalmia Recorded as an Outcome or Outcome Measure	No. of Sympathetic Ophthalmia Cases	Sympathetic Ophthalmia Rate (%)	Time after Index Injury at Which Sympathetic Ophthalmia Occurred
Colyer et al (2008)[18]	35	25	1	Yes	0	0	*
du Toit et al (2008)[19]	889	3	491	Yes	0	0	*
Savar et al (2009)[20]	649	8	3	Yes	Primary repair, 3	Primary repair, 0.462	2 mos, 12 mos, and NA
Zhang et al (2009)[21]	NA (4796 estimate)	172 (mixed group with primary enucleations and eviscerations)		Yes	Primary repair, 18	0.334	26 days–22 yrs
Bauza et al (2013)[22]	136	11	0	Yes	0	0	*
Chang et al (2016)[23]	167	0	32	Yes	0	0	*
Ji et al (2017)[24]	134	14	0	Yes	0	0	*
Gensheimer et al (2021)[25]	35	9	10	Yes	0	0	*

NA = not available.

Table 4. Sympathetic Ophthalmia Rates after Primary Repair versus Primary Eye Removal (Enucleation or Evisceration)

	Anticipated Absolute Effects (95% Confidence Interval)				
Outcomes	*Risk with Primary Repair*	*Risk with Primary Enucleation or Primary Evisceration*	**Relative Effect (95% Confidence Interval)**	**No. of Participants (Studies)**	**Certainty of the Evidence (Grading of Recommendations, Assessment, Development, and Evaluations)***
Risk of SO	1.5 per 1000 (0−3.3)	0.5 per 2000 (0−2.1)	ARR, −0.0010 in favor of eye removal (0.0011 to −0.0031)	7620 (8 retrospective observational studies)	low†

ARR = absolute risk reduction; SO = sympathetic ophthalmia.
*Grading of Recommendations, Assessment, Development, and Evaluations Working Group grades of evidence: high certainty = very confident that the true effect lies close to that of the estimate of the effect; moderate certainty = moderately confident in the effect estimate, in that the true effect is likely to be close to the estimate of the effect, but a possibility exists that it is substantially different; low certainty = confidence in the effect estimate is limited in that the true effect may be substantially different from the estimate of the effect; very low certainty = very little confidence in the effect estimate in that the true effect is likely to be substantially different from the estimate of effect.
†Low certainty as based on observational data, downgraded by 1 level for risk of bias resulting from missing data, but upgraded back to low because residual confounding from variation in injury severity would favor SO in removed eyes (opposite to what was seen).

SO cases in patients who had undergone primary repair of an estimated 4796 patients undergoing primary repair (based on assumption of conservative management not being practiced). No other cases of SO were reported in the other studies. Results are presented in Table. 3.

When all included studies were pooled, the estimated SO rate was 0.12% (95% confidence interval [CI], 0.00%−0.25%) after OGI (Table 4). Of 779 patients who underwent primary enucleation or primary evisceration, no SO cases were reported, resulting in a pooled SO estimate of 0.05% (95% CI, 0.00%−0.21%). For primary repair, the pooled estimate of SO was 0.15% (95% CI, 0.00%−0.33%).

The estimated ARR using a random effects model was −0.0010 (in favor of eye removal; NNT, n = 1000), with a 95% CI from 0.0011 (in favor of primary repair) to −0.0031 (in favor of eye removal; Fig 2). The NNT derived from the 95% CI of ARR indicated that at least 323 injured eyes would need to be removed to prevent 1 case of SO (1 / 0.0031).

Discussion

This systematic review reports data from 7620 OGIs from 8 retrospective observational studies. The objective of this study was to refine the known rate of SO occurring after OGI associated with primary repair and with primary enucleation or primary evisceration. We found a pooled SO rate for all included studies of 0.12% (95% CI, 0.00%−0.25%) after OGI. No patient who underwent primary

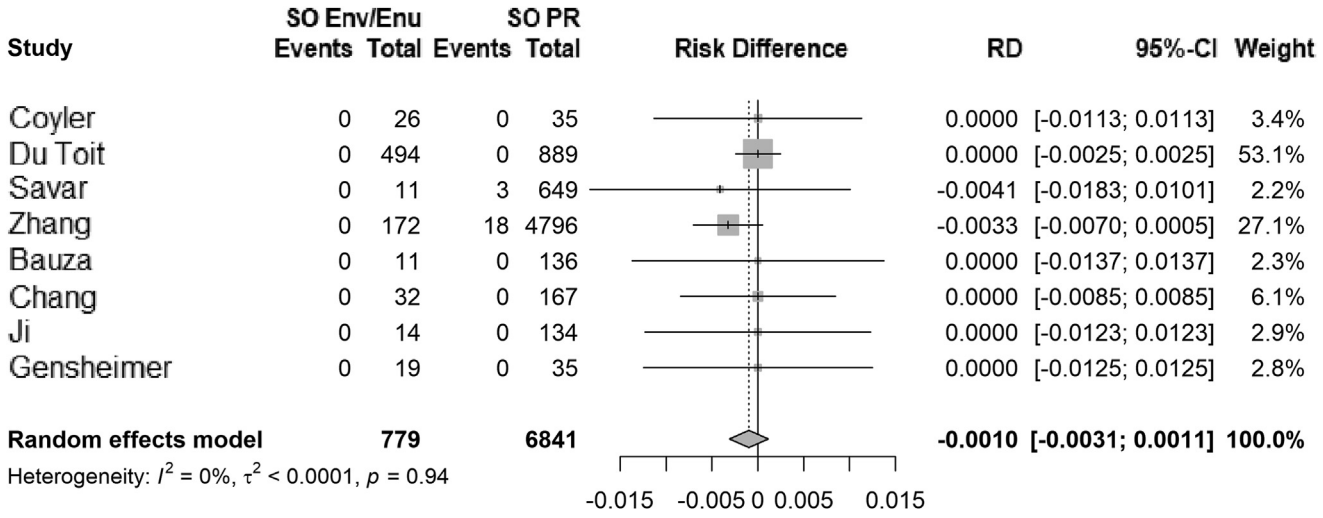

Figure 2. Forest plot reporting the absolute risk reduction of sympathetic ophthalmia (SO) developing among patients who underwent primary repair versus those who underwent primary eye removal. Note that follow-up reporting was heterogenous: 5 of 8 studies reported mean or median follow-up of more than 3 months,[18–20,22,23] 1 study did not report follow-up times,[24] 1 study reported a range of SO presentations between 2 and 24 months,[21] and 1 study reported that 60% of patients were followed-up for more than 30 days.[25] CI = confidence interval; Enu = enucleation; Env= evisceration; PR = primary repair; RD = risk difference.

enucleation or primary evisceration was reported as demonstrating SO. When meta-analyzed with a zero cell value of 0.05%, this rate was estimated as 0.05% (95% CI, 0.00%−0.21%). After primary repair, the estimated rate was 0.15% (95% CI, 0.00%−0.33%). The rates in the patient group who underwent primary repair compared with the group who underwent primary enucleation or primary evisceration were not significantly different. The precision and therefore the clinical relevance of negative results are indicated by CIs, and a 95% CI of the ARR indicated an NNT (that is, the number of primary enucleations and primary eviscerations to prevent 1 case of SO) of at least 323.

Bellan[26] estimated that it would be necessary to perform between 908 and 9999 prophylactic primary enucleations after trauma to prevent 1 case of visual loss resulting from SO, based on the assumptions that the SO rate was between 3.1% and 0.28%, that 64% of patients respond to steroids and enucleation, that 66% of patients respond to immunosuppressives, and that enucleation prevents all cases of sympathetic ophthalmia. Our assessment was based on the relative risk in the two treatment groups based on all available published data, but our estimate of 323 cases as the lower limit of the 95% CI to prevent 1 case of SO would extrapolate, using Bellan's figures, to needing to remove 6218 eyes to prevent 1 case of visual loss, a figure higher than Bellan's lower estimate. The upper limit of our estimate is that no benefit to eye removal exists, and, therefore, no number of eyes could be removed to prevent 1 case of visual loss.

A systematic review in 2022 reported a rate of SO after OGI of 0.19%, which is comparable with our overall risk of SO, but was not stratified according to management strategy.[8] An additional narrative review in 2022 suggested, given improved efficacy in modulating intraocular inflammation associated with SO, that even the most severe OGI should have attempted repair.[9] With continued development of targeted biologic agents, a new class of additional immunosuppressant agents is available now for those with ocular inflammation secondary to SO, further reducing the risk of visual loss compared with Bellan's[26] estimates and reinforcing the argument for attempted repair. A large cohort study of 130 patients with SO treated with modern immunomodulatory therapy or enucleation of the inciting eye reported a final VA of 6/15 or better in 63.1% of patients.[27]

This review did not find a significantly increased rate of SO when OGIs were managed with primary repair. However, these data were not stratified according to injury severity, and the morbidity of primary enucleation or primary evisceration versus the morbidity associated with SO in the current era of immunomodulators was not considered.

The authors highlight that the included studies were conducted in populations with index presentations between 1995 and 2015. The techniques for OGI primary repair and the techniques for primary enucleation or primary evisceration have not altered drastically within this time. The paradigm shift during this period has been the introduction of immunomodulatory therapies for SO treatment[7]; however, the introduction of these therapies should not change the rate of SO, only its management.

Study Limitations

The authors acknowledge limitations of this study. Observational studies are limited in their ability to draw causal relationships, in this case between primary surgical procedures and the later development of SO, because the baseline characteristics of each group may be different, meaning that the Grading of Recommendations, Assessment, Development, and Evaluations assessment is of low-certainty evidence (Table 4); however, the authors acknowledge that these surgical groups will be different, with more severe injuries likely to undergo primary enucleation or evisceration, which would be expected to bias the results toward more SO in the eye removal groups, which was not seen.[28] The addition of ocular trauma scoring, along with the type of trauma, in an analyzable format to future studies of SO risk may decrease this potential bias. Surgical timing, surgeon experience and training (which may affect the modulation of uveal tissue left exposed to immune response), and surgical approach also were not reported in a way to allow analysis.

In addition, as highlighted in the risk of bias analysis, issues with the reporting of outcome data and intervention data were present. For example, in the largest study included, Zhang et al,[23] we relied on an estimated number of patients with OGI undergoing primary repair. Because of the high risk of bias resulting from missing data evaluated for this study, a moderate risk of overall bias was assessed with the ROBINS-I tool, and the Grading of Recommendations, Assessment, Development, and Evaluations assessment was of a low certainty of evidence.[21]

Finally, length of follow-up also is variable and is reported variably, being specified as means, medians, ranges, or in one case, not at all. Classical teaching is that $>$ 80% of cases of SO occur within 3 months of injury, although others suggest that the time to onset may be longer, with one study finding a mean time to onset of 384 days (standard deviation, 538 days).[19,29] Retrospective studies always demonstrate variable time to follow-up, patients with disease are more likely to return for follow-up than those without, and, for conditions like SO with long potential onset times, mean values may be skewed (median values are preferred). Gensheimer et al[25] reported a loss to follow-up for some local population military members and civilians, meaning that cases may have been missed, but the other included studies did not report specific patient groups with incomplete follow-up. Nonetheless, given that SO onset may occur many years after trauma, cases occurring after the last follow-up remain a risk, and, therefore, rates may be underestimated, although we do not expect a differential effect on removed compared with repaired eyes (the primary study question).

Conclusions

The model-based rate of SO after primary enucleation and primary evisceration as treatments for OGI was 0.05% (95%, CI 0.00%−0.21%), compared with a rate of 0.15% (95% CI, 0.00%−0.33%) after primary repair.[20–22] We did not find evidence that eye removal reduced the risk of SO

but estimate that, if such an effect exists, at least 323 eyes would need to be removed to prevent 1 case of SO, a limited justification for eye removal based on SO risk, although the certainty of evidence is low. The potential morbidity associated with eye removal (psychological impact, quality-of-life issues, phantom eye syndrome), as well as loss of vision, therefore, must be balanced against the rarity of SO and its treatability with advanced immunomodulatory therapy.[9,30]

With rates of SO of 0.15% after primary repair, prospective randomized studies to examine the effect of primary repair compared with eye removal on SO rate would not be practical because of the very large number of patients required. Population-level studies remain the best way to assess rates of SO in OGI populations further with different management strategies. These studies may report ocular trauma scoring, surgical timing, and clear surgical technique reporting to allow analysis of these factors on SO risk.

Footnotes and Disclosures

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Conception and design: Patterson, Kedzierski, McKinney, Ritson, McLean, Gu, Colyer, McClellan, Miller, Justin, Hoskin, Cavuoto, Leong, Ascarza, Woreta, Miller, Caldwell, Gensheimer, Williamson, Dhawahir-Scala, Shah, Coombes, Sundar, Mazzoli, Woodcock, Watson, Kuhn, Halliday, Gomes, Agrawal, Blanch

Analysis and interpretation: Halliday

Data collection: Patterson, Kedzierski, McKinney, Ritson, McLean

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Abbreviations and Acronyms:
ARR = absolute risk reduction; **CI** = confidence interval; **NNT** = number needed to treat; **OGI** = open-globe injury; **SO** = sympathetic ophthalmia.

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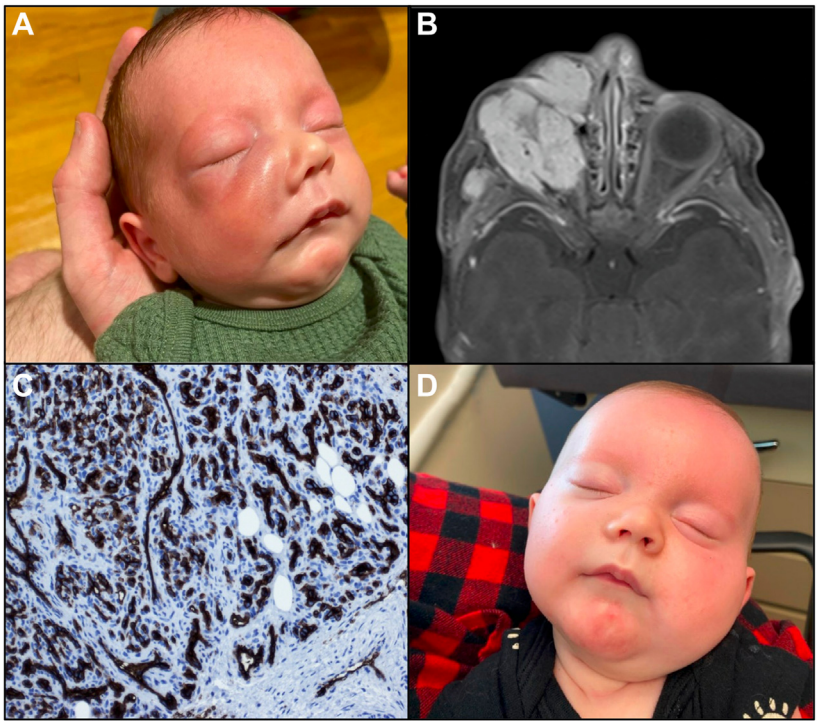
Pictures & Perspectives



Unusual Deep Infantile Hemangioma Presentation with Orbital Involvement

A 45-day-old boy presented with 2 weeks of worsening right-sided facial swelling concerning for dacryocystocele. The patient did not respond to a 7-day course of intravenous clindamycin. Physical examination revealed periorbital and maxillary swelling without erythema or induration (**A**). Magnetic resonance imaging revealed a 3×3×2–cm lobulated mass in the right inferior orbit with proptosis and partial encasement of the optic nerve (**B**). Given concerning features on imaging, biopsy was performed, showing tightly packed capillaries organized into lobules and endothelial cells staining for glucose transporter 1 (GLUT-1) (**C**). This confirmed the lesion as an infantile hemangioma; oral propranolol was initiated with significant improvement (**D**). (Magnified version of Figure **A**-**D** is available online at www.aaojournal.org).

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