

Risk Factors for Enucleation Following Open Globe Injury: A 17-Year Experience

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Purpose: At the time of open globe injury (OGI), it may be difficult for clinicians to predict which eyes are at highest risk for requiring enucleation. We performed a 17-year retrospective cohort study to report outcomes and risk factors for enucleation following open globe injury to better aid clinicians counseling patients at OGI diagnosis.

Methods: A retrospective cohort study of all patients who presented to the University of Michigan with open globe injury (OGI) and were surgically managed between January 2000 and July 2017 was conducted. At least 30 days of follow-up was required. All eyes that ultimately underwent enucleation following OGI were identified and their clinical course analyzed. The main outcome measured was the rate of enucleation after OGI.

Results: There were 587 eyes meeting inclusion criteria. The mean patient age was 40.75 ± 25.1 (range 1–91). 441/585 (75.4%) patients were male. Average follow-up time was 1029.9 ± 1285.9 days. 116/587 eyes (19.8%) required enucleation after OGI, with 81.9% undergoing enucleation less than 30 days from injury. In enucleated eyes, the mean presenting logMAR vision was 2.91 ± 0.47 (Snellen equivalent between hand motion and light perception). The most common mechanism of injury requiring enucleation was globe rupture, 89/116 (76.7%), with 14/116 (12.1%) penetrating injuries and 13/116 (11.2%) perforating injuries. The mean age of patients that underwent enucleation was 45.6 ± 22.5 (range 3–91).

Conclusion: Open globe injuries are often visually devastating and a significant number of cases ultimately require enucleation. Despite emergent closure within 24 hours, 19.8% of eyes managed for OGI at our institution required eventual enucleation. 81.2% of these eyes required enucleation within 30 days of injury. Wound length greater than 10 mm, uveal prolapse, higher zone of injury, IOFB, and RAPD were identified as risk factors that predict future need for enucleation.

Keywords: ocular trauma, open globe repair, globe rupture, eye injury, enucleation

Introduction

Open globe injuries (OGI) are potentially visually devastating injuries that are often treated at tertiary referral centers. The current standard of care is to attempt to close the globe within 24 hours to prevent endophthalmitis. Even with timely closure of the wounds, OGI often leaves patients with impaired vision, with only 16% to 33% of eyes that present with no light perception (NLP) vision regaining any vision at all.^{1,2} A subset of patients ultimately require enucleation due to a combination of poor vision, infection, and a painful eye. Previous studies estimate that 7% to 28% of eyes with ocular trauma undergo enucleation.^{3–12} Currently, after an OGI, secondary enucleation is more commonly performed than primary enucleation.^{1,3,13} This allows time for any potential salvage of vision and for patients to come to terms with their vision loss following OGI and process this significant event in their lives.

When patients present with these devastating injuries, ophthalmologists are tasked with counseling them regarding the management and prognosis of the OGI. Difficulty exists for clinicians in counseling patients at the time of OGI diagnosis regarding their visual prognosis and potential need for enucleation in the future, as there is a paucity of data surrounding the risk factors that predict the need for enucleation. When encountering a patient with an OGI, physicians often employ the Ocular Trauma Score (OTS), a tool designed to predict a patient's postoperative visual potential after an OGI.¹⁴ It

utilizes globe rupture and perforating injury as two key predictors of poor visual outcome along with initial visual acuity (VA), retinal detachment (RD), endophthalmitis and the presence of a relative afferent pupillary defect (RAPD). The OTS is a useful tool to predict a patient's subsequent visual potential and for counseling the patient regarding expectations following globe closure. However, the OTS cannot be used to address factors such as risk for phthisis and chronic pain following globe closure, which may result in the patient requiring enucleation in the future.

The current incidence of enucleation in the United States is 2.8 per 100,000 persons.⁴ This includes enucleation for several ocular pathologies including glaucoma, neoplasia and endophthalmitis. A large retrospective study has found that 62.5% of enucleations are due to trauma.¹⁵ Attempts to investigate the epidemiology and sociodemographic populations related to OGI found age over 85, young males, elderly females, and patients of African-American descent are at increased risk for OGI.^{4,16,17} Furthermore, enucleation after OGI was associated with male gender, Black race, and age 21–40.^{4,17} There have been several investigations risk factors for various outcomes for patients with OGI.^{2,13,14,18–24} These have looked at a variety of outcomes most often visual acuity, but also included retinal detachment and hypotony. Enucleation as an outcome for OGI has seldomly been evaluated. Risk factors previously found to be associated with enucleation are rupture injury, endophthalmitis, phthisis, and poor preoperative best-corrected visual acuity.^{3,4,13} The purpose of this study was to develop a better understanding of the risk factors that predict enucleation following open globe injury.

Methods

A single-center retrospective cohort study of all patients who presented to the University of Michigan hospital system with an open globe injury was conducted. The University of Michigan Institutional Review Board (IRB) approved this study prior to data collection and waived the need for informed consent. This study was compliant with the Health Insurance Portability and Accountability Act (HIPAA) and adherent to the tenants of the Declaration of Helsinki.

A chart review of all patients who presented to the University of Michigan hospital system with an OGI and were surgically managed between January 2000 and July 2017 was conducted. Inclusion criteria included the diagnosis and management of an OGI during the predetermined timeframe and a minimum follow-up time of 30 days. Exclusion criteria consisted of a follow-up time less than 30 days (231), if globe repair was performed at an outside hospital (101), inadequate records (69), death prior to globe repair (3), self-sealing injuries that did not require surgical management (2), and iatrogenic OGIs that were the result of an intraoperative complication during an ophthalmic surgery (1).

The University of Michigan hospital has a standardized protocol for the evaluation and management of patients with OGI. All patients with OGI are initially evaluated in the emergency department (ED) with a complete ophthalmic examination of both eyes and computed tomography (CT) of the orbits. Once OGI is identified the injured eye is protected with a shield, and the patient is administered intravenous antibiotics. The patient is also provided with pain medication, anti-emetics, and a tetanus booster as needed. Surgical repair of the OGI by the eye trauma team is completed urgently within 24 hours of injury unless there are medical contraindications, need for other lifesaving surgeries, or there has been a delay in presentation to the ED. The intraoperative examination of OGI determines the surgical procedure and extent of exploration. It generally aims to remove any foreign bodies and close the wound. If the IOFB is discovered in the posterior segment, the surgeon may decide to remove the IOFB secondarily and will deliver intravitreal antibiotics at globe closure. Fungal prophylaxis may be added as well if there is suspicion for a contaminated wound or dirty IOFB. On postoperative day one, topical antibiotics, corticosteroids and cycloplegic eyedrops are initiated. If there is physician preference the postoperative antibiotics may be administered per os (PO). Patients are not routinely admitted to the hospital for intravenous antibiotics following their globe repair. After surgery, patients are counseled about the importance of future eye protection, especially for the uninjured eye. The patient is then encouraged to maintain close follow-up with the particular care needed based on the post-repair residual pathology. In the rare instance, where on exam it was discovered that there appears to be insufficient tissue remaining for globe closure, the trauma team will request an oculoplastics consultation to evaluate the patient for primary enucleation or evisceration.²⁵

In order to assess patient outcomes, patient data was extracted from the electronic medical record (Table 1). The extracted data consisted of patient demographics including age and gender, presenting characteristics including presenting VA, mechanism of injury, previous ocular surgery, time to presentation, IOP on presentation, RAPD, intraocular foreign body (IOFB), zone of injury, wound length, lens status, lens disruption including implant disruption, uveal prolapse, vitreous

Table I Number of Patients Presenting with Variables Used in Univariate Analysis

Variable		Number of Patients Requiring Enucleation N=116	Number of Patients Not Requiring Enucleation N=469	p-value
Injury mechanism				0.0005
Penetrating		14 (12.1%)	96 (20.5%)	
Perforating		13 (11.2%)	105 (22.4%)	
Rupture		89 (76.7%)	268 (57.1%)	
Previous ocular surgery				0.0272
	Yes	38 (32.8%)	107 (22.9%)	
	No	78 (67.2%)	361 (77.1%)	
Time to Presentation				0.0266
	<24 hours	107 (93.0%)	398 (85.2%)	
	>24hrs	8 (7.0%)	69 (14.8%)	
RAPD				<0.0001
	Yes	31 (63.3%)	61 (21.1%)	
	No	18 (36.7%)	228 (78.9%)	
IOFB				0.0750
	Yes	11 (9.5%)	75 (16.0%)	
	No	105 (90.5%)	393 (84.0%)	
Zone of Injury				<0.0001
	I	25 (21.6%)	244 (52.0%)	
	II	18 (15.5%)	118 (25.2%)	
	III	73 (62.9%)	107 (22.8%)	
Wound Length				<0.0001
	<5mm	3 (2.9%)	142 (33.1%)	
	5–10mm	10 (9.8%)	125 (29.1%)	
	11–15mm	25 (24.5%)	72 (16.8%)	
	16–20mm	16 (15.7%)	35 (8.2%)	
	>20mm	48 (47.1%)	55 (12.8%)	
Lens Status at Time of Injury				0.0327
	Phakic	84 (73.0%)	387 (82.9%)	
	Pseudophakic	30 (26.1%)	74 (15.9%)	
	Aphakic	1 (0.9%)	6 (1.3%)	
Lens Disruption Including Implant Disruption				0.6717
	Yes	50 (44.6%)	217 (46.9%)	
	No	62 (55.4%)	246 (53.1%)	
Uveal Prolapse				<0.0001
	Yes	105 (91.3%)	296 (63.2%)	
	No	10 (8.7%)	172 (36.8%)	

(Continued)

Table 1 (Continued).

Variable		Number of Patients Requiring Enucleation N=116	Number of Patients Not Requiring Enucleation N=469	p-value
Vitreous hemorrhage at time of wound closure				0.1539
	Yes	48 (43.2%)	165 (36.0%)	
	No	63 (56.8%)	294 (64.1%)	
Intraocular inflammation with or without hypopyon at time of presentation				0.0079
	Yes	5 (4.4%)	62 (13.3%)	
	No	108 (95.6%)	405 (86.7%)	
Retinal Detachment				0.0119
	Yes	39 (35.5%)	110 (23.8%)	
	No	71 (64.5%)	353 (76.2%)	
Endophthalmitis				0.6027
	Yes	6 (5.2%)	19 (4.1%)	
	No	110 (94.8%)	441 (95.9%)	
Time to Surgery				0.3587
	<24 hours	99 (85.3%)	380 (81.7%)	
	>24 hours	17 (14.7%)	85 (18.3%)	
Vitrectomy at time of open globe repair				0.6833
	No	91 (79.8%)	365 (77.8%)	
	Weck-Cel	20 (17.5%)	77 (16.4%)	
	Anterior Vitrectomy	0	6 (1.3%)	
	Posterior Vitrectomy	3 (2.6%)	21 (4.5%)	
Lensectomy				0.9438
	Yes	10 (8.8%)	40 (8.6%)	
	No	104 (91.2%)	427 (91.4%)	
Presenting VA				<0.0001
	<20/400	2 (2.3%)	99 (25.2%)	
	≥20/400	87 (97.7%)	294 (74.8%)	

Abbreviations: RAPD, relative afferent pupillary defect; IOFB, intraocular foreign body.

hemorrhage at time of wound closure, intraocular inflammation, RD, endophthalmitis, and management including time to surgery, lensectomy, and vitrectomy at time of globe repair. For statistical analysis of VA, the Snellen VA collected was converted to logarithm of the minimum angle of resolution (logMAR) equivalents to simplify the analysis with its continuous scale. Count fingers (CF), hand motion (HM), light perception (LP), and no light perception (NLP) were adapted to logMAR values of 1.85, 2.3, 2.75 and 3.2, respectively.²⁶ When classifying the specific details of a patients OGI, the Ocular Trauma Classification Group definitions were used to describe zones of injury.²⁷ Zone 1 includes the entire cornea including corneoscleral limbus. Zone 2 refers to the area of the sclera within 5 mm of the limbus. Zone 3 refers to the area posterior to the first 5 mm of the sclera from the limbus. The highest zone of injury was used to classify the injury.

All eyes that ultimately underwent enucleation following OGI were identified and their clinical course analyzed. The main outcome measured was the number of eyes requiring removal after OGI regardless if enucleation or evisceration was performed. Looking at both enucleation and evisceration would provide increased insight to the risk factors predicting the need to remove an eye after OGI independent of the method employed to remove it. We defined primary enucleation/evisceration as enucleation/evisceration occurring as the first surgery after OGI without first successfully closing repairing the globe, while secondary enucleation/evisceration was defined as enucleation/evisceration performed after a successful globe repair. For convenience, we have chosen to refer to the removal of an eye as enucleation throughout the remainder of the paper.

Using univariate logistic regression, the potential risk factors for enucleation after OGI were assessed for statistical significance. Those that were found to be statistically significant in univariate modeling were then assessed for their significance in a multivariable logistic regression model. A final multivariable model was then selected by keeping the most significant risk factors using the backward selection method. For factors that have more than two levels, both Type III p-values that are to assess the overall effect of a variable and p-values for pairwise comparisons were included. All tests were two-sided and a p-value of less than 0.05 was considered statistically significant. All model analyses were performed in SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Between January 2000 and July 2017 there were 933 patients diagnosed and treated for OGI at University of Michigan hospital system. There were 585 patients with 587 eyes that met inclusion criteria for this study (Table 2). The majority of patients were male (441/585, 75.4%), and had a mean age of 40.7 ± 25.1 years (range 1–99) at time of injury. On presentation, patients with OGI had a mean logMAR VA of 2.11 ± 1.01 (Snellen equivalent between counting fingers and hand motion visual acuity). The information and clinical characteristics regarding time from injury to presentation at our center was available in 581/585 (99.3%) of patients. Most patients had no previous ocular surgery before OGI (439/585, 75.0%) (Table 1). Globe closure in most cases was within 24 hours of OGI (479/581, 82.4%). Most patients (77/102) that were operated on after 24 hours from time of injury presented to our institution after the 24-hour window. Their delay in presentation was due to several factors including first presenting to other institutions that were not equipped to surgically manage open globe injuries and subsequent transfer of their care to our hospital. 4 cases had an unknown timing from injury to globe repair. Mean follow-up time for all patients was 1029.9 ± 1285.9 days with a median follow-up time of 433 days (range 3–6660 days).

Of the 587 eyes that met inclusion criteria, 19.8% (116/587) required enucleation. The average presenting logMAR vision of patients that ultimately underwent enucleation was of 2.91 ± 0.47 (Snellen equivalent between light perception and no light perception). Presenting visual acuity was not able to be collected in 26/116 patients, often limited by patients' abilities or willingness to participate with exam. 81.9% of enucleated eyes were enucleated within 30 days of OGI. The

Table 2 Demographics and Characteristics of Patients Presenting with Open Globe Injury

	Total Eyes	Requiring Enucleation	No Enucleation	p-value
Open Globe Injuries	587	116	471	
Male*	441/585 (75.4%)	82/116 (70.7%)	359/469 (76.5%)	0.1899
Female*	144/585 (24.6%)	34/116 (29.3%)	110/469 (23.5%)	
Average Age	40.7 ± 25.1 yrs	45.9 ± 22.4 yrs	39.5 ± 25.6 yrs	0.0055
Presenting logMAR VA	2.11 ± 1.01	2.91 ± 0.47	1.93 ± 1.01	<0.0001
Presenting Snellen Equivalent VA	Between Count Fingers & Hand Motion	Between Light Perception & No Light Perception	Count Fingers	N/A
Mean Follow Up	1029.9 ± 1285.9 Days	935.1 ± 1371.0 Days	1053.1 ± 1264.5 Days	0.0170

Notes: *The change in denominator in these rows reflects the number of patients that presented with OGI, as there were patients that had bilateral OGI on presentation.

mechanisms of injury were identified and classified in Table 1. The most common mechanism of OGI that required enucleation was globe rupture (76.7%), followed by penetrating injuries (12.1%) and then perforating injuries (11.2%).

Details regarding the rationale for surgery was gathered from several locations in the patients' chart including clinic notes, ED consult notes, surgical consent forms, operative notes, and outgoing letters from the surgeon. Most of the eyes had multiple reasons for enucleation recorded. These included indications for surgery as well as other additional benefits that may be provided by having the eye removed, such as prophylaxis for the small risk of sympathetic ophthalmia. The most common reasons for enucleation listed were a painful eye (65.5%), followed by sympathetic ophthalmia prophylaxis (25.9%), and globe rupture beyond repair (17.4%). Other reasons included endophthalmitis (3.4%), fungal keratitis (0.9%), and orbital cellulitis (0.9%).

There were 26 eyes (4.4%) in our cohort that had primary enucleation. In 20 of our primary enucleation cases, the patient's ocular trauma did not leave behind enough viable tissue remaining for an open globe repair, which necessitated primary enucleation. 6 of these eyes were damaged due to intentional self-harm with a gunshot wound to the head. The remaining 6 eyes that underwent primary enucleation were due to the patients' preference for primary enucleation after counseling about available treatment options including globe repair. Their decision was heavily influenced by considerations regarding their increased age, all over 75 years-old at time of injury, presentation with NLP vision and previous medical history. Three of the patients had a history of penetrating keratoplasty and their OGI was due to damage to their corneal transplant. These patients opted to undergo enucleation and avoid the possibility of requiring multiple surgeries due to concern for their increased risk of undergoing general anesthesia with cardiovascular and pulmonary comorbidities that included CHF and COPD. Two other patients were previously blind in the eye that had OGI. The first patient was blind due to radiation damage from maxillary sinus carcinoma treatment and chose to have the eye enucleated while undergoing other cosmetic repairs of his face. The other was a patient with dementia who was not well aware of her surroundings and had a phthisical eye due to self-inflicted damage. Her durable power of attorney decided to pursue primary enucleation due to the functional status of the patient and their concern for the patient's ability to care for the repaired eye. The final patient who elected to have primary enucleation was a candidate for an open globe repair however she was concerned about the possibility of undergoing additional surgeries and after counseling and shared decision-making decided that she would like to have her eye enucleated.

An IOFB was present in 88/587 of OGIs during our study period. Only 11/116 of the enucleated eyes (9.5%) had an IOFB. 5/11 of these eyes underwent immediate pars plana vitrectomy (PPV) and IOFB removal at presentation. 6 of the IOFB were metallic, the remaining were a wooden tree branch, vegetable matter, plastic, bone and one non-metallic but unknown material. 5 of these IOFB were caused by projectiles from a gun (handgun, BB gun, and potato gun). 4 were projectiles from a tools striking hard materials. The remaining foreign bodies were a projectile released from highly pressurized oxygen and a branch introduced on impact in a car accident.

In our cohort of OGIs, there were 2 patients that developed sympathetic ophthalmia during the study period. They were both patients with extensive ocular injury. The first was a patient with previous ocular trauma who presented to our emergency department for initial medical management 8 days after OGI with prolapsed uvea, vitreous prolapse into anterior chamber and vitreous hemorrhage. He developed sympathetic ophthalmia two weeks after globe repair. The second was a previously healthy patient that presented with an OGI complicated by a metallic IOFB and *Clostridium bifermentans* endophthalmitis who developed sympathetic ophthalmia 2 months after globe repair.

Univariate logistic regression analysis was performed to assess for risk factors and protective factors that predict eventual enucleation (Table 3). Significant variables were then considered and modeled in a multivariable logistic regression including injury mechanism, previous ocular surgery, time to presentation (hours), RAPD, IOFB, zone of injury, wound length, lens status, uveal prolapse, intraocular inflammation with or without hypopyon at time of presentation, retinal detachment, age (years), and presenting VA LogMAR. After selection, the final multivariable model includes 5 variables: RAPD, IOFB, zone of injury, wound length, and uveal prolapse (Table 4). Our multivariable model identified that the presence of RAPD [odds ratio (OR) 2.93, 95% confidence interval (CI) 1.42–6.05, $p=0.0037$], IOFB (OR 2.97, 95% CI 1.17–7.53 $p=0.0222$), higher zone of injury (zone 3 vs 1, OR 3.05, 95% CI 1.71–5.44, $p=0.0002$; zone 2 vs 1 OR 0.98, 95% CI 0.48–1.98, $p=0.9537$; zone 3 vs 2, OR 3.12, 95% CI 1.67–5.83, $p=0.0004$; global

Table 3 Univariate Analysis of Risk Factors for Enucleation Following OGI

Variable	Level	Odds Ratio	95% CI Lower	95% CI Upper	p-value	Type III p-value
Injury mechanism	Penetrating vs Rupture	0.44	0.24	0.81	0.0082	0.0007
	Perforating vs Rupture	0.37	0.20	0.70	0.0019	
Previous ocular surgery	Yes vs no	1.64	1.06	2.56	0.0282	
Time to presentation (hours)	>24h vs <24h	0.43	0.20	0.92	0.0306	
RAPD	Yes vs no	6.44	3.37	12.28	<0.0001	
IOFB	Yes vs no	0.55	0.28	1.07	0.0787	
Zone of injury	2 vs 1	1.49	0.78	2.84	0.2263	<0.0001
	3 vs 1	6.66	4.01	11.06	<0.0001	
Wound length	5–10mm vs <5mm	3.79	1.02	14.07	0.0468	<0.0001
	11–15mm vs <5mm	16.44	4.80	56.27	<0.0001	
	16–20mm vs <5mm	21.64	5.97	78.40	<0.0002	
	>20mm vs <5mm	41.31	12.35	138.14	<0.0003	
Lens status pre-OGI	Pseudophakic vs phakic	1.87	1.15	3.04	0.0117	0.0386
	Aphakic vs phakic	0.77	0.09	6.46	0.8080	
Lens disruption including implant disruption	Yes vs no	0.91	0.60	1.38	0.6718	
Uveal prolapse	Yes vs no	6.10	3.11	11.99	<0.0001	
Vitreous hemorrhage at time of wound closure	Yes vs no	1.36	0.89	2.07	0.1548	
Intraocular inflammation with or without hypopyon at time of presentation	Yes vs no	0.30	0.12	0.77	0.0123	
Retinal detachment	Yes vs no	1.76	1.13	2.75	0.0126	
Endophthalmitis	Yes vs no	1.28	0.50	3.29	0.6034	
Time to surgery from injury	>24h vs <24h	0.77	0.44	1.35	0.3598	
Vitreotomy at time of globe repair	Weck-Cel vs no	1.04	0.61	1.79	0.8824	0.8413
	Anterior vitrectomy vs no	<0.001	<0.001	>999.999	0.9837	
	Posterior vitrectomy vs no	0.57	0.17	1.96	0.3754	
Lenectomy	Yes vs no	1.03	0.50	2.12	0.9434	
Age (Years)	Continuous	1.01	1.00	1.02	0.0144	
Presenting VA LogMAR	Continuous	13.35	6.59	27.07	<0.0001	
Presenting VA	<20/400 vs ≥20/400	16.48	3.99	68.13	0.0001	

Notes: Bolded rows within the table denote statistically significant risk factors and their associated odds ratios and p-values.

Abbreviations: RAPD, relative afferent pupillary defect; IOFB, intraocular foreign body.

Table 4 Multivariable Analysis of Risk Factors for Enucleation Following OGI

Risk Factor	Level	Odds Ratio	95% CI Lower	95% CI Upper	p-value	Type III p-value
RAPD	Yes vs no	2.929	1.419	6.047	0.0037	
IOFB	Yes vs no	2.966	1.168	7.531	0.0222	
Zone of injury	Zone II vs Zone I Injury	0.979	0.483	1.984	0.9537	<0.0001
	Zone III vs Zone I Injury	3.053	1.712	5.442	0.0002	
	Zone III vs Zone II*	3.117	1.666	5.833	0.0004	
Wound Length	>10mm vs ≤10mm	8.832	4.279	18.227	<0.0001	
Uveal Prolapse	Yes vs no	3.79	1.678	8.563	0.0014	

Notes: *Comparison between Zone III vs Zone II injury was obtained by changing the reference level of the multivariable model.

Abbreviations: RAPD, relative afferent pupillary defect; IOFB, intraocular foreign body.

$p < 0.0001$), increased wound length (>10mm vs ≤10 mm OR 8.83, 95% CI 4.28–18.23, $p = < 0.0001$) and uveal prolapse (OR 3.79, 95% CI 1.68–8.56, $p = 0.0014$) were risk factors for eventual enucleation.

Discussion

OGI are visually devastating injuries that are a leading cause of blindness in working aged individual.¹³ The standard of care for OGIs in the United States is to attempt primary repair of the injured eye regardless of the extent of injury. A subset of eyes with OGIs ultimately undergo enucleation. By collecting outcome of OGIs requiring enucleation, this study identifies risk factors that clinicians can use to predict which eyes have the highest probability of eventual enucleation.

In our study, 19.8% of eyes with an OGI eventually required enucleation, consistent with the previously reported rates of between 7% and 28%.^{3–12} Our study also confirmed that the majority of globe repairs after OGI are successful since most required enucleation were secondary enucleations rather than primary enucleation, supporting the practice of primary repair and observation without need for immediate enucleation.^{1,3} Although not measured in our study, the literature also describes that up to 20% of eyes with NLP vision at presentation may improve to LP or better after initial treatment, which also supports attempts at repairing all open globe injuries and avoiding primary enucleation if possible.^{4,28–36}

Our cohort had a primary enucleation rate of 4.4%. This is consistent with the generally reported rates between 0% and 7.4%.^{3,5–9} In some specialized settings, such as in the military, there are reports of rates as high as 25%.¹⁰ As a level 1 trauma and referral center, we see some of the most severe ocular trauma in our region. Additionally, as opposed to other academic centers, our institution has a robust oculoplastic surgery department that consistently maintains a faculty member on call to care for patients requiring primary enucleations. In the majority of our primary enucleation cases, the patients had extensive ocular trauma that did not leave behind enough viable tissue for an open globe repair. This was usually related to the mechanism of injury such as 6 cases with ocular damage due to intentional self-harm with a gunshot wound to the head. The remaining 6 eyes that underwent primary enucleation were due to the patients' preference for primary enucleation after counseling about available treatment options including globe repair.

We have found that many of the eyes that were secondarily enucleated had more than one indication for enucleation documented in their evaluation notes and their operative and consent documentation. The most common indication for enucleation was a blind painful eye which is consistent with other retrospective studies investigating indications for enucleation.^{1,3,4} Their pain was often apparent soon after the initial globe repair and the majority of patients (81.9%) had their secondary enucleation performed within 30 days of their injury. This highlights the importance of maintaining close follow-up with patients after their globe closure.

Sympathetic ophthalmia prophylaxis was listed as one of several reason to enucleate eyes in 25.9% of enucleated patients' documentation. It was always listed as a secondary reason in all but one case. It must be noted that the overall risk of sympathetic ophthalmia is significantly low, reported to be between 0.2% and 0.5%.³ This is supported by our cohort's 0.3% rate of developing sympathetic ophthalmia. Of note, the patients that developed sympathetic ophthalmia

had extensive ocular injury. Our documentation of sympathetic ophthalmia prophylaxis did not reflect a primary surgical indication. It reflected a potential additional benefit of enucleation that was often discussed while comprehensively counseling patients about the risks and benefits of enucleation to thoroughly educate them during the shared decision-making process. Due to the low risk of sympathetic ophthalmia demonstrated by our cohort and other related studies, as well as recent advances in understanding sympathetic ophthalmia's immune mediated pathophysiology, and improvements in immunosuppressive medical management it no longer seems necessary to enucleate eyes for prophylaxis.^{3,37,38} After OGI, patients should be counseled about the risks of sympathetic ophthalmia and the need for lifetime surveillance for with close follow-up and early diagnosis and treatment patients have good prognosis.^{37,39–41}

The mechanism of globe injury seemed to play an important role in future need for enucleations. In our cohort, eyes that had a globe rupture injury were more than 6 times more likely to be enucleated than penetrating or perforating injuries (Table 1). Globe ruptures being a greater risk for enucleation is consistent with findings in other studies describing OGIs as a risk factor for enucleation, but the rupture injuries in our cohort demonstrated a much greater magnitude of risk than in the other studies.^{3,4} It is also worth mentioning that a globe rupture injury has been used as one of the variables in the Ocular Trauma Score and is most notably the variable with the largest weight by points.¹⁴

The demographics of our study's cohort was consistent to other similar studies with working-age males at the highest risk for both OGI and enucleation.^{1,3,4,16} This continues to highlight the need for ocular protection in this population and the general population as well.

In our study, we recognized several clinical signs which if present at the time of diagnosis were risk factors for future enucleation. The presence of uveal prolapse was a significant risk factor for enucleation, OR 3.79 (95% CI 1.68–8.56, $p=0.0014$). Generally, uveal prolapse can be noted at the initial examination of the eye and aid in clinicians formulating their initial counseling. However, it should be noted that there are cases of scleral rupture in which the uvea may prolapse under the conjunctiva and tenons thereby remaining hidden until globe exploration. Clinicians should take this into consideration when initially describing their exam findings and preparing patients for next steps.

The finding of a RAPD, OR 2.93 (95% CI 1.42–6.05, $p=0.0037$), as well as IOFB and zone of injury, which are discussed in detail below, are other risk factors that are often apparent to the diagnosing ophthalmologist. These exam findings can be used collectively to counsel patients regarding the severity of their injury and the fact that they have a poor visual prognosis. It may be reasonable to inform patients with these risk factors when consenting them for open globe repair that there is a chance that they may require enucleation in the future to allow the patient to begin processing this outcome.

Wound length greater than 10 mm was the risk factor with the highest odds of eventual enucleation, OR 8.83 (95% CI 4.28–18.23, $p<0.0001$). This factor is only able to be determine intraoperatively when measuring the extent of injury. Clinicians can consider discussing with patients with large wounds in the pre- and post-operative period.

An OGI with a higher zone of injury was found to be a risk factor associated with future enucleation. Injuries to zone 3 compared to zone 1 had an increased risk of enucleation with an OR 3.05 (95% CI 1.71–5.44, $p=0.0002$). A zone 2 injury compared to zone 1 injury when analyzed alone was found to be insignificant, however when grouped and modeled with zone 3 injury this was found to be statistically significant. Zone 3 injury compared to zone 2 injury analysis was also obtained by changing the reference level of the multivariable model from zone 1 to zone 2 and showed an increase in enucleation with a zone 3 injury OR 3.12 (95% CI 1.67–5.83, $p=0.0004$). Our study supports the previous mentioned association between an OGI with zone 3 injury and a poorer prognosis and highlights higher zone of injury at presentation as a risk factor for enucleation.^{2,13,18,20}

An IOFB was present in 14.7% of OGIs during our study period. Only 9.5% of the enucleated cohort presented with IOFBs. 5/11 of the enucleated eyes with IOFB had undergone immediate PPV with IOFB removal at presentation. Previous reports have suggested that the presence of an IOFB is protective against enucleation compared with penetrating injuries.⁴ Our study found that an IOFB was a risk factor for enucleation with an OR 2.97 (95% CI 1.17–7.53, $p=0.0222$). IOFBs are associated with significant visual consequences through multiple mechanisms including endophthalmitis, which carries its own risks for enucleation. There are no standardized recommendations for timing of foreign body removal in OGI management. The uncertainty centers on posterior segment IOFBs which typically require the involvement of a vitreoretinal surgeon to extract the foreign material by means of a pars plana vitrectomy (PPV). Several studies advocate for the expedited removal

of the IOFB by recommending a vitreoretinal surgeon join the surgeon performing the primary globe repair highlighting the lower rates of endophthalmitis.^{42,43} Others have found no difference in endophthalmitis rates between primary and secondary removal.^{44,45} In our study, 6/11 eyes with IOFB that were eventually enucleated did not have vitrectomy at the time of globe repair. Further research can assess whether timing of IOFB removal can impact the risk of enucleation.

In this study, we did not differentiate between enucleation and evisceration. We were primarily investigating the risk factors that would necessitate the removal of an eye with a traumatic injury, regardless of which procedure was ultimately performed. However, there are several factors that may influence a surgeon's decision to pursue a particular approach. In our cohort, prophylaxis for sympathetic ophthalmia was often discussed with patients as a benefit of removing their damaged eye. Enucleation may be preferred as prophylaxis for sympathetic ophthalmia because there is a theoretical increased risk with evisceration due to the retained ocular tissue. However, as mentioned above, the overall risk of sympathetic ophthalmia is significantly low, and we have immunosuppressive medical management available. Furthermore, this theoretical risk after evisceration is strongly debated in the literature, requiring further research.^{3,37}

Although rare, there are several case studies that report eviscerated eyes containing a variety of different unsuspected malignancies.^{46–48} Properly evaluating eyes that experienced OGI presents challenges due to the trauma. When eyes must be removed, performing enucleations can potentially avoid the risk of leaving behind tissue with unknown malignancy. If evisceration is to be pursued it should be done with a careful evaluation of the ocular surface as well as appropriate preoperative imaging if the eye cannot be examined properly.

Other reasons that may favor enucleation are severe trauma to the scleral shell, better post-operative pain control, improved aesthetic outcomes, and differences in complications between the two procedures.^{49–54} Supporters of evisceration point to finer cosmetic outcomes, superior prosthesis motility, and fewer implant-related complications.^{38,48,55} There is not yet a clear consensus on which procedure to pursue.³⁸ Ultimately, at this point surgeon preference or institution protocol that may heavily influence the method of treatment.

There are several limitations to our study. The main one being its formulation as a single-center retrospective cohort study in which its outcomes may be influenced by the providers at our institution, as well as hospital-specific practice patterns that are responsible for OGI management. Furthermore, due to the extended period over which the data was collected, there may have been changes to surgical technique and medical management that may have influenced outcomes. Other limitations include a selection bias due to our inclusion criteria and losses to follow-up. Future coordinated multicenter prospective studies as well as meta-analysis can continue to elucidate the best practices surrounding OGI repairs to better counsel patients regarding their risk for enucleation.

Our study exhibits several strengths as well. The data was collected at a large academic institution, which serves as a tertiary referral center for ocular trauma in its respective region. This helped collect a cohort with OGIs of varying complexities to serve as a foundation for our study. The data was also collected over a 17-year period with lengthy patient follow-up that provided insight to complications that may develop over significant time periods.

Conclusion

Open globe injuries (OGI) are often visually devastating and in a significant number of cases ultimately require enucleation. Despite emergent closure within 24 hours, 19.8% of eyes managed for OGI at our institution required eventual enucleation. 81.9% of these eyes required enucleation within 30 days of injury. Wound length greater than 10 mm, uveal prolapse, higher zone of injury, IOFB, and RAPD were identified as risk factors that predict future need for enucleation.

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Disclosure

The authors report no conflicts of interest in this work.

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