Glaucoma Following Penetrating Ocular Trauma: A Cohort Study of the United States Eye Injury Registry

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• PURPOSE: To evaluate associations between baseline structural and functional ocular characteristics and the risk of developing posttraumatic glaucoma after penetrating ocular injury.
• DESIGN: Prospective cohort study
• METHODS: Data from the United States Eye Injury Registry (USEIR) were obtained from a total of 3,627 patients who experienced penetrating ocular injury. The risk of posttraumatic glaucoma and associated structural and functional ocular risk factors was estimated.
• RESULTS: The risk of developing posttraumatic glaucoma was 2.67%. The development of glaucoma was independently associated with several baseline characteristics including advancing age (relative risk 1.02/yr 95% confidence interval [1.00, 1.03]), lens injury (1.56 [1.03, 2.35]), poor baseline visual acuity (2.59 [1.62, 4.14]), and inflammation (3.02 [1.52, 6.02]).
• CONCLUSIONS: This study provides an estimate for the risk of developing glaucoma after penetrating ocular injury in a large cohort of patients and determined several factors that are significantly associated with the development of post-traumatic glaucoma, including advancing age, lens injury, poor visual acuity, and intraocular inflammation. (Am J Ophthalmol 2005;139:100-105. © 2005 by Elsevier Inc. All rights reserved.)

Several epidemiologic studies have been performed examining the risk of developing posttraumatic glaucoma after blunt ocular injury and angle recession.[1–4] Although several studies have previously determined the risks and risk factors for poor visual outcome after penetrating ocular trauma,[5–15] to our knowledge no study has determined the overall risk of developing glaucoma and its risk factors after penetrating ocular injury. In the assessment of individuals after ocular trauma it is important to identify and treat secondary conditions such as post-traumatic glaucoma that may adversely affect visual outcome to minimize any additional damage that may occur.[16]

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METHODS

Data from the United States Eye Injury Registry (USEIR) was obtained from 3,627 patients who experienced penetrating ocular trauma, as defined by the Ocular Trauma Classification nomenclature[17,18] between 1988 and January 2003. The USEIR was founded in 1988 with the purpose of collecting information on serious ocular injury. The USEIR was developed based on the Eye Injury Registry of Alabama, which was in operation for 6 years before the development of the USEIR. Currently, 39 of 50 states in the United States contribute to the USEIR, along with 15 other countries. Data are collected from hospitals, emergency rooms, and physicians' offices on all types of trauma determined as serious eye trauma, defined as trauma that may potentially result in permanent structural or functional damage. A standardized reporting form is filled out on the initial examination of a patient with ocular trauma. Information regarding demographics, the nature and location of injury, the extent of ocular injury assessed both structurally and functionally, and any initial surgical interventions are recorded on the initial visit after the traumatic injury. At 6 months, an additional form is filled out encompassing information regarding the structural and functional ocular outcomes resulting from the initial trauma and any additional procedures that have occurred. The data are then collected at the central office of the USEIR in Birmingham, Alabama, and stored in the USEIR database. Only data from subjects who had both forms completed were used in this analysis. Approval for the purposes of reporting data were obtained for this study, and the University of Alabama at Birmingham Human Sub-

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jects Committee approved the methods of data collection and analysis. All identifying characteristics were removed from the data before analysis.

The primary outcome of interest was post-traumatic glaucoma within the 6-month follow-up period. Cases were defined as having developed post-traumatic glaucoma within the 6-month follow-up period based on the 6-month report form as determined by the physician submitting the form based on the presence of elevated intraocular pressure, optic disk, or visual field abnormality consistent with glaucoma. Specific information on IOP, number of medications, need for glaucoma surgery, optic disk, or visual field changes are not recorded in the USEIR database. Baseline factors used in the analyses were obtained from the initial examination form including data collected on demographic information, baseline visual function, and the results of the initial slit-lamp examination. Specific parameters used as independent variables in the analysis were age, gender, race, eye injured, ocular tissue injured (cornea, scleral, iris, lens, retina, vitreous, retina, choroidal), and baseline visual acuity; the presence of a relative afferent pupillary defect (RAPD), vitreous hemorrhage, choroidal hemorrhage, retinal detachment, hyphema, intraocular foreign body (IOFB), or inflammation; and whether the injured eye had a previous abnormality before the penetrating ocular injury.

Statistical Analysis: Logistic regression was used to calculate the association between the presence of baseline demographic characteristics, baseline ocular functional measures, ocular structures involved in the initial injury and the risk of developing glaucoma using relative risks (RRs) and 95% confidence intervals. To determine the set of baseline parameters that demonstrated significant, independent associations with post-traumatic glaucoma, several logistic regression models were evaluated. First, the association between glaucoma and each parameter was estimated separately (Model 1—crude model). Individual multivariable models were then evaluated for factors associated with anterior segment involvement (corneal involvement, scleral involvement, iris involvement, lens involvement, and hyphema), posterior segment involvement (vitreous involvement, choroidal involvement, retinal detachment, vitreous hemorrhage, choroidal hemorrhage), baseline visual functional parameters (initial acuity worse than 20/200, the presence of a relative papillary defect, eye abnormality before injury), and a group of parameter associated specifically with inflammatory secondary injury (infection, inflammation). From these separate full models, only those variables that demonstrated significant, independent associations in each model were retained in reduced models. Finally, the parameters in each of these reduced models identified as being independently associated with glaucoma were included in a single multivariable model. In the context of this model, only those variables that retained their statistical significance were maintained in the final model. Age was also retained in the models at all steps because it was the only demographic feature significantly association with the development of glaucoma. P values $\leq .05$ were considered statistically significant.

RESULTS

OF THIS COHORT OF 3,627 PATIENTS WHO EXPERIENCED serious penetrating ocular involvement, 97 developed post-traumatic secondary glaucoma, yielding an overall cumulative incidence of 2.67% over the 6-month follow-up for each subject. Demographic information obtained from the initial examination is presented for the patients who eventually developed post-traumatic glaucoma and those who did not in Table 1. Only increasing age was associated with increased rates if developing glaucoma in the 6 months after penetrating ocular injury.

Functional prognostic factors are presented in Table 2. Baseline visual acuity that was worse than 20/200 was significantly associated with the development of post-traumatic glaucoma, with a 4% risk of eventually developing glaucoma. Additionally, the patient having a previous ocular abnormality in the injured eye was significantly associated with post-traumatic glaucoma. More details concerning the nature of the predisposing ocular condition are not collected in the USEIR database.

The risk and crude relative risk of developing post-traumatic glaucoma associated with baseline injury to various anterior segment and posterior segment structures, in addition to specific signs of secondary injury (hyphema, inflammation, or infection) based on the initial assessment are presented in Table 3. Damage to the iris or lens, vitreous hemorrhage, and inflammation on baseline examination were associated with a significantly greater risk of developing glaucoma after penetrating ocular involvement in this univariate analysis. The presence of hyphema and retinal detachment were of borderline significance.

Table 4 presents the staged multivariable logistic regression models for the risk factors associated with the developing of glaucoma after penetrating ocular injury. Model 1 contains the univariate relative risk. Model 2 contains relative risk adjusted for the group interactions and the final model, Model 3, contains those parameters that remain significant when all interactions are taken into account. The parameters independently associated with the development of glaucoma included advancing age, lens injury, poor visual acuity, and intraocular inflammation when adjusted for the effect of the other terms in the model. The presence of intraocular inflammation on baseline examination had the highest independent association of any ocular characteristic with the development of post-traumatic glaucoma.

TABLE 1. Risk of Glaucoma After Penetrating or Perforating Eye Trauma Associated With Demographic Characteristics

	No Glaucoma* n (%)	Glaucoma† n (%)	Glaucoma† Risk‡	RR (95% CI)	*P* Value
Age, mean (SD)	28.9 (17.6)	37.4 (18.5)	—	**1.02 (1.01, 1.03)**	**<.0001**
Sex					
Female	462	16	0.03	1.00	
Male	3,068	81	0.03	1.02 (1.01, 1.03)	.3352
Race					
Caucasian	1,979	52	0.03	1.00	
African American	555	15	0.03	0.86 (0.48, 1.52)	.9254
Unknown	996	30	0.03	1.00 (1.00, 0.63)	.5624
Injured Eye					
Left	1,737	48	0.03	1.00	
Right	1,689	47	0.03	1.01 (0.67, 1.51)	.9723
Both	89	2	0.02	0.71 (0.17, 2.94)	.6404
Unknown	12	0	0.00		

Significant risk in bold face. CI = confidence interval; RR = relative risk.
*n = 3,530.
†n = 97.
‡Risk per 100.

TABLE 2. Risk of Glaucoma After Penetrating or Perforating Eye Trauma Associated With Baseline Functional Parameters

	No Glaucoma* n (%)	Glaucoma† n (%)	Glaucoma† Risk‡	RR (95% CI)	*P* Value
Baseline visual acuity					
>20/200	1,851	25	0.01	1.00	
<20/200	1,679	72	0.04	**3.09 (1.95, 4.86)**	**<.0001**
Eye before Injury					
Normal	3,407	123	0.03	1.00	
Abnormal	88	9	0.07	**2.71 (1.36, 5.38)**	**.0044**
RAPD					
No	3,338	91	0.03	1.00	
Yes	192	6	0.03	1.14 (0.50, 2.61)	.7529

Significant risk in bold face. CI = confidence interval; RAPD = relative afferent pupillary defect; RR = relative risk.
*n = 3,530.
†n = 97.
‡Risk per 100.

DISCUSSION

THIS STUDY FOUND AN OVERALL INCIDENCE OF POST-traumatic glaucoma after penetrating ocular involvement of 2.67% and identified several risk factors associated with the development of post-traumatic glaucoma. Using a multivariable logistic regression model, advancing age, lens injury, baseline visual acuity below 20/200, and anterior chamber inflammation were independently associated with the development of post-traumatic glaucoma. Although several studies have focused on the development of glaucoma after blunt ocular injuries and specific traumatic sequelae such as traumatic hyphema and angle recession, to the best of our knowledge, no previous study has examined the risks and associated risk factors for the development of post-traumatic glaucoma after penetrating ocular trauma.

Both retinal detachment and hyphema were of borderline significance. Given that the weakness inherent in the reporting characteristics used by the USEIR (outlined later) may result in an underestimation of the true relative risks, these borderline associations may warrant further study to determine whether a relationship exists.

Initial IOP is usually low after penetrating or perforating injury, but after wound closure, glaucoma may develop

TABLE 3. Risk of Glaucoma After Penetrating or Perforating Eye Trauma Associated With Baseline Structural Parameters

	No Glaucoma*	Glaucoma†			
	n (%)	n (%)	Risk‡	RR (95% CI)	*P* Value
Anterior segment injury					
Cornea					
No	759	22	0.03	1	
Yes	2,771	75	0.03	0.94 (0.58, 1.51)	.7834
Sclera					
No	1,791	50	0.03	1	
Yes	1,739	47	0.03	0.97 (0.65, 1.44)	.8767
Iris					
No	2,717	64	0.02	1	
Yes	813	33	0.04	**1.70 (1.11, 2.58)**	**.0138**
Lens					
No	2,138	44	0.02	1	
Yes	1,392	53	0.04	**1.82 (1.22, 2.71)**	**.0034**
Hyphema					
No	2,520	61	0.02	1	
Yes	1,010	36	0.03	1.46 (0.97, 2.20)	.0737
Posterior segment injury					
Vitreous involvement					
No	1,972	46	0.02	1	
Yes	1,558	51	0.03	1.39 (0.93, 2.07)	.1049
Choroidal involvement					
No	3,260	86	0.03	1	
Yes	270	11	0.04	1.37 (0.66, 2.82)	.1889
Retinal involvement					
No	3,144	77	0.04	1	
Yes	511	20	0.06	1.58 (0.97, 2.60)	.0669
Vitreous hemorrhage					
No	2,340	52	0.02	1	
Yes	1,190	45	0.04	**1.68 (1.13, 2.50)**	**.0112**
Choroidal hemorrhage					
No	3,039	491	0.02	1	
Yes	77	20	0.04	1.51 (0.73, 3.10)	.2655
Secondary injury					
IOFB					
No	2,615	72	0.03	1	
Yes	913	25	0.03	1.00 (0.63, 1.57)	.9842
Inflammation					
No	3,417	88	0.03	1	
Yes	113	9	0.07	**2.93 (1.48, 5.83)**	**.0021**
Infection					
No	3,392	92	0.03	1	
Yes	138	5	0.04	1.33 (0.54, 3.26)	.5399

Significant risk in bold face. CI = confidence interval; IOFB = intraocular foreign body; RR = relative risk.
*n = 3,530.
†n = 97.
‡Risk per 100.

because of structural alterations from the injury, blockage of the trabecular meshwork, or secondary responses such as inflammation. Several potential etiologies exist for the development of glaucoma after penetrating eye injury. Inflammation, especially with a shallow or flat anterior chamber, may lead to synechial closure of the angle. Alternatively, angle closure may occur due to iris bombe, synechial closure at the pupillary margin, or lens swelling. The trabecular meshwork may also become occluded by blood cells from a hyphema, inflammatory debris, lens particles, or ghost cells associated with long-standing vitreous hemorrhage. In the case of retained IOFBs,

TABLE 4. Multivariable Logistic Regression Models (significant relative risk bolded)

	Model 1	Model 2	Model 3
	RR (95% CI)	RR (95% CI)	RR (95% CI)
Age (per year)	**1.02 (1.01, 1.03)**	**1.02 (1.01, 1.03)**	**1.02 (1.00, 1.03)**
Anterior segment parameters			
Corneal involvement	0.94 (0.58, 1.51)	0.75 (0.45, 1.25)	
Scleral involvement	0.97 (0.65, 1.44)	0.92 (0.59, 1.41)	
Iris involvement	**1.70 (1.11, 2.58)**	1.41 (0.89, 2.23)	
Lens involvement	**1.82 (1.22, 2.71)**	**1.69 (1.10, 2.60)**	**1.56 (1.03, 2.35)**
Hyphema	1.46 (0.97, 2.20)	1.36 (0.88, 2.11)	
Posterior segment parameters			
Vitreous involvement	1.39 (0.93, 2.07)	0.68 (0.29, 1.59)	
Retinal detachment	1.58 (0.97, 2.60)	1.30 (0.76, 2.22)	
Choroidal involvement	1.37 (0.66, 2.82)	1.24 (0.38, 3.98)	
Vitreous hemorrhage	**1.68 (1.13, 2.50)**	2.14 (0.91, 5.04)	1.29 (0.86, 1.93)
Choroidal hemorrhage	1.51 (0.73, 3.10)	0.95 (0.25, 3.60)	
Baseline functional parameters			
Baseline visual acuity (<20/200)	**3.09 (1.95, 4.86)**	**3.03 (1.91, 4.79)**	**2.59 (1.62, 4.14)**
RAPD	1.14 (0.50, 2.61)	0.85 (0.37, 1.96)	
Eye abnormality before injury	**2.71 (1.36, 5.38)**	**2.31 (1.16, 4.60)**	1.51 (0.72, 3.21)
Inflammatory-related parameters			
IOFB	1.00 (0.63, 1.57)	0.98 (0.62, 1.55)	
Inflammation	**2.93 (1.48, 5.83)**	**2.90 (1.46, 5.78)**	**3.02 (1.52, 6.02)**
Infection	1.33 (0.54, 3.26)	1.21 (0.49, 3.01)	

Significant risk in bold face. CI = confidence interval; IOFB = intraocular foreign body; RAPD = relative afferent pupillary defect; RR = relative risk.
*n = 3,530.
†n = 97.
‡Risk per 100.

prolonged ocular retention of foreign bodies containing ferrous metals may lead to siderosis and iron staining of the trabecular structures. The presence of an IOFB was not found to be a significant risk factor in our series, likely because, in the vast majority of these cases, an IOFB was removed on initial examination if detected. Additionally, secondary glaucoma due to ghost cell and lens rupture may not be well evaluated in this data set because it is likely that this material would have been removed with the 6-month follow-up period.

This study evaluated a cohort of patients suffering a penetrating ocular injury using prospectively planned systematic survey methods and can be used to determine the independent risk factors associated with the development of glaucoma. A strength of this study is that data from the USEIR is obtained from several geographic regions, and thus it is likely these results may be more generalizable than studies examining specific ocular injuries in selected or localized populations.

This study has several limitations. First, to encourage greater participation, detailed ocular characteristics are not included in the USEIR reporting forms, and thus structural and functional ocular characteristics such as the extent and character of lens, iris, and angle injury could not be accessed in greater detail. Also, more detailed information regarding past ocular history was not obtained, so the exact nature of preexisting conditions, although rare in this cohort, is unknown. Additionally, there may be some variation in reporting characteristics from different sites, because glaucoma was defined by the judgment of the treating physician; however, any misclassification of either exposure or disease from different reporting physicians should yield a nondifferential misclassification and therefore bias the point estimates of relative risk toward the null so that our relative risk estimates may underestimate the true relative risk. For any reporting errors that may exist in the USEIR database to confound the relationship between independent risk factors and the development of post-traumatic glaucoma, these reporting errors would have to be associated with this relationship. There is little reason to believe this is the case. Thus, although this study has probably accurately identified many significant risk factors, factors of borderline significance may have been overlooked. Also, precise information regarding the type of glaucoma that developed and the degree of nerve damage is not available in this data set. Lastly, data from patients following ocular trauma are not collected beyond 6 months after involvement; thus, the long-term incidence and associated risk factors cannot not be determined from this data set, and this report applies only to early-onset posttraumatic glaucoma.

In summary, using data obtained from a large cohort of patients who suffered penetrating ocular injury, our study found that glaucoma rarely developed, with an incidence of 2.67%. Several baseline risk factors were identified that were significantly and independently associated with the development of glaucoma, including advancing age, lens injury, baseline visual acuity less than 20/200, and anterior chamber inflammation. This information may prove useful in determining which individuals may be at greater risk for developing posttraumatic glaucoma after penetrating ocular injuries.

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