Ischemic Optic Neuropathy in Cardiac Surgery

Incidence and Risk Factors in the United States from the National Inpatient Sample 1998 to 2013

Daniel S. Rubin, M.D., Monica M. Matsumoto, B.A., Heather E. Moss, M.D., Ph.D., Charlotte E. Joslin, O.D., Ph.D., Avery Tung, M.D., F.C.C.M., Steven Roth, M.D., F.A.R.V.O.

CME This article has been selected for the Anesthesiology CME Program. Learning objectives and disclosure and ordering information can be found in the CME section at the front of this issue.

ABSTRACT

Background: Ischemic optic neuropathy is the most common form of perioperative visual loss, with highest incidence in cardiac and spinal fusion surgery. To date, potential risk factors have been identified in cardiac surgery by only small, single-institution studies. To determine the preoperative risk factors for ischemic optic neuropathy, the authors used the National Inpatient Sample, a database of inpatient discharges for nonfederal hospitals in the United States.

Methods: Adults aged 18 yr or older admitted for coronary artery bypass grafting, heart valve repair or replacement surgery, or left ventricular assist device insertion in National Inpatient Sample from 1998 to 2013 were included. Risk of ischemic optic neuropathy was evaluated by multivariable logistic regression.

Results: A total of 5,559,395 discharges met inclusion criteria with 794 (0.014%) cases of ischemic optic neuropathy. The average yearly incidence was 1.43 of 10,000 cardiac procedures, with no change during the study period ($P = 0.57$). Conditions increasing risk were carotid artery stenosis (odds ratio, 2.70), stroke (odds ratio, 3.43), diabetic retinopathy (odds ratio, 3.83), hypertensive retinopathy (odds ratio, 30.09), macular degeneration (odds ratio, 4.50), glaucoma (odds ratio, 2.68), and cataract (odds ratio, 5.62). Female sex (odds ratio, 0.59) and uncomplicated diabetes mellitus type 2 (odds ratio, 0.51) decreased risk.

Conclusions: The incidence of ischemic optic neuropathy in cardiac surgery did not change during the study period. Development of ischemic optic neuropathy after cardiac surgery is associated with carotid artery stenosis, stroke, and degenerative eye conditions. **(Anesthesiology 2017; 126:810-21)**

What We Already Know about This Topic

- Ischemic optic neuropathy is the most common form of perioperative visual loss, with highest incidence in cardiac and spinal fusion surgery
- This study determined the preoperative risk factors for ischemic optic neuropathy using the National Inpatient Sample, a database of inpatient discharges for nonfederal hospitals in the United States

What This Article Tells Us That Is New

- Development of ischemic optic neuropathy after cardiac surgery is associated with carotid artery stenosis, stroke, and degenerative eye conditions

PERIOPERATIVE visual loss is a rare but devastating complication of nonocular surgery. Ischemic optic neuropathy (ION) is the most common mechanism, with reported cardiac surgery incidence ranging from as high as 1.3 to 0.06%, and most recently estimated at 0.086%.[1–3] There is painless vision loss affecting either the anterior optic nerve or the posterior optic nerve. Anterior optic nerve injury is more prevalent in cardiac surgical procedures, whereas posterior optic nerve injury is more common in posterior spinal fusion surgery.[2,4] ION has been well studied in spinal fusion, with risk factors of age, obesity, male sex, blood loss, increased surgical duration, type of surgical positioning frame, and low colloid/crystalloid ratio for fluid

Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org). Presented in part at the Upper Midwest Neuro-ophthalmology Group Annual Meeting in Chicago, Illinois, July 22, 2016.

Submitted for publication August 3, 2016. Accepted for publication January 5, 2017. From the Department of Anesthesia and Critical Care (D.S.R., A.T.), and Department of Anesthesia and Critical Care, The Center for Health and the Social Sciences (S.R.), The University of Chicago Medicine, Chicago, Illinois; Pritzker School of Medicine of the University of Chicago, Chicago, Illinois (M.M.M.); Department of Ophthalmology and Visual Science, Department of Neurology and Rehabilitation, College of Medicine, University of Illinois at Chicago, Chicago, Illinois (H.E.M.); Department of Ophthalmology and Visual Science, College of Medicine, Division of Epidemiology and Biostatistics, School of Public Health, University of Illinois at Chicago, Chicago, Illinois (C.E.J.); and Department of Anesthesiology, Department of Ophthalmology and Visual Sciences, College of Medicine, University of Illinois at Chicago, Chicago, Illinois (S.R.). Current position: Department of Ophthalmology, Byers Eye Center, Stanford University, Palo Alto, California (H.E.M.).

<zdoi;10.1097/ALN.0000000000001533>

therapy.[5–7] A recent study suggests that ION in spinal fusion has decreased during the past 15 yr.[8]

ION in cardiac surgery has been less studied and may result from a different mechanism. A 1982 case series suggested hypotension, hypothermia, and complement activation as possible risk factors.[9] Three retrospective single-institution cohort studies did not replicate these findings but rather identified other risk factors including severe peripheral vascular disease, cardiopulmonary bypass (CPB) time, packed erythrocyte units transfused, lowest hemoglobin, nonpacked erythrocyte transfusion, and preoperative angiogram less than 48 h before the procedure.[1,2,4] However, these studies are limited by small size, with a combined total of only 34 cases and thus may lack generalizability. Moreover, they are now greater than 15 yr. Since then cardiac surgery has changed considerably, with 25% fewer coronary artery bypass graft (CABG) procedures, and a significant increase in left ventricular assist device insertion.[10,11] Using the National Inpatient Sample (NIS), Shen *et al.*[3] performed the largest analysis to date of ION in cardiac surgery and identified male sex and an increased Charlson index score as risk factors. However, the study did not address factors specific to cardiac surgery such as comorbidities indicative of severe vascular disease, type of cardiac surgery, and use of CPB.

Chronic ophthalmic disease is a possible risk factor due to local hemodynamic impairment known to be associated with glaucoma, age-related macular degeneration, and diabetic retinopathy.[12,13] A recent study supported this notion by demonstrating increased prevalence of diabetic retinopathy in diabetics with incident microvascular ocular motor palsies.[14] On a broader level, a large body of literature supports associations between vascular diseases of the eye with both acute and chronic cerebrovascular diseases that persist after accounting for potentially common causes such as systemic vascular disease.[15]

Based upon previous studies, we hypothesized that specific patient medical conditions are associated with ION after cardiac surgery and that these are distinct from ION after posterior spine fusion surgery. Moreover, we also hypothesized that specific surgical elements such as CABG and use of CPB would also be associated with ION. To test our hypotheses, we analyzed the NIS to identify risk factors associated with ION after cardiac surgery. Additionally, because of changes in procedure volume in cardiac surgery during the study period, we evaluated the incidence and trends in ION after cardiac surgery involving CABG, heart valve repair or replacement surgery, and left ventricular assist device procedure.

Materials and Methods

Data Source

The NIS of the Healthcare Cost and Utilization Project is directed by the Agency for Healthcare Research and Quality (AHRQ, Rockville, Maryland).[16] It is an approximate 20% stratified survey sample of nonfederal U.S. hospital discharges derived from a typical hospital discharge abstract. The NIS includes age, race, total charges, hospital characteristics including teaching status and location, discharge disposition, and 25 diagnostic and 15 procedural codes defined in the International Classification of Diseases, Ninth Revision–Clinical Modification (ICD-9-CM).[17] Beginning in 2012, the NIS was redesigned to improve national estimates, by sampling all participating hospitals rather than a subset.[16] To ensure accurate weighting of the sample across multiple years, AHRQ has provided updated discharge weights for the years 1998 to 2011. We used these updated trend weights, combined with the survey function for all patient-level analysis and regressions, as previously described.[8] The University of Chicago and University of Illinois (Chicago, Illinois) Institutional Review Boards deemed the study exempt from Institutional Review Board review since there are no patient identifiers.

Data Classification

Our retrospective analysis included inpatient discharges of adults aged 18 yr or older with ICD-9-CM procedure codes for CABG (36.10 to 36.16, 36.17, 36.19), valve repair or replacement (35.1 to 35.14, 35.2 to 35.28), and left ventricular assist device (37.66) procedures from 1998 to 2013. Insertion of an intraaortic counter pulsation balloon pump (37.61) and CPB (39.61, 39.62) were included as secondary procedures. There were no cases of ION in heart transplant, atrial and ventricular septal defect repair, and congenital heart surgery in those aged 18 yr or older; therefore, these procedures were excluded.

To compare the incidence of ION in a nonsurgical inpatient population, we analyzed patients with significant coronary artery disease requiring a percutaneous intervention (PCI). Coronary artery disease was chosen since the majority of ION cases were associated with the CABG procedure. This group consisted of adults aged 18 yr or older with an ICD-9-CM procedure code for percutaneous coronary intervention and placement of either a bare-metal stent (36.06) or drug-eluting stent (36.07). Patients with a concurrent procedure code for CABG, valve repair or replacement, or left ventricular assist device procedure on the same admission were excluded from the PCI cohort. Surgical and PCI patients discharged with a principal or secondary diagnostic ICD-9-CM code of ischemic optic neuropathy (377.41) were considered to have developed ION during the hospitalization.

Patient and Surgical Characteristics

Patient characteristics analyzed included age (years, continuous variable), sex, length of hospital stay (days), yearly inflation-adjusted total hospital charges, type of admission (elective and emergent), discharge status (routine, short-term hospital, home health care, died, and other), and race.[18] Potential risk factors were identified before analysis based upon previous case series, large database reviews, and case reports as recommended in the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[19] See Supplemental Digital Content 1, Table, http://links.lww.com/ALN/B374 for ICD-9-CM patient comorbidity codes. We studied obesity, obstructive sleep apnea, smoking, hypertension, diabetes type 1 or 2 uncomplicated, diabetes with renal manifestations, diabetes with neurologic manifestations, diabetic retinopathy, diabetes with peripheral circulatory disorders, hypertensive retinopathy, glaucoma, age-related macular degeneration, cataract, peripheral vascular disease, coronary artery disease, carotid artery stenosis, stroke (postoperative, acute, embolic, and thrombotic), blood transfusion, hyperlipidemia, atrial fibrillation, congestive heart failure (systolic and diastolic), pulmonary hypertension, and anemia. Degenerative eye conditions were included because they may predispose to ION.[20,21] To investigate concern that chronic ophthalmic conditions could appear falsely associated with ION due to increased frequency of eye exams in affected patients, cataract was also studied as a patient comorbidity as it should not act as a risk factor for ION.

Statistical Analysis

The primary outcome was ION during an admission for one of the three cardiac surgical procedures, CABG, valve repair or replacement, or left ventricular assist device or for PCI. AHRQ trend weights and the survey functions of STATA (StataCorp LLC, USA) were used for all national estimates and regressions.[8] Dividing individual survey estimates from the total count can lead to rounding variation in the NIS data set, as seen in the total number of ION cases when compared to cases of ION for the different cardiac procedures. Data were complete except for race (n = 1,261,433 [23%]), type of admission (n = 1,692,552 [30%]), age (n = 433 [0.01%]), length of stay (n = 185 [less than 0.01%]), and discharge status (n = 7,316 [0.1%]). Due to high rates of missing data for race and type of admission, they were not included in the univariable and multivariable analyses.

Patient characteristics for all cardiac procedures were compared for 1998 to 2013 using the national estimates and reported with 95% CI. We used chi-square with a second-order Rao–Scott correction to detect differences in the incidence of ION in the different cardiac surgery procedures and differences in cardiac surgery procedure rates during the study period. The mean incidence of ION in cardiac surgery and PCI was compared using an adjusted Wald test.[22] Rates of cardiac surgical procedures were calculated as procedures per million adults (greater than 18 yr old) in the U.S. population using U.S. Census data.[23] A univariate logistic regression was performed for patient characteristics and for primary and secondary cardiac procedures to identify covariates associated with ION. Characteristics and procedures with $P \leq 0.2$ were then included in a multivariable logistic regression. Those with $P \leq 0.05$ in the multivariable logistic regression were considered significant, and the odds ratio (OR), 95% CIs, and *P* value were reported. Changes in the temporal trend of ION incidence were assessed using multivariable logistic regression, modeling year as a continuous variable and including primary cardiac procedures to account for changes in procedure volume over time.

The variance inflation factor (VIF) examined collinearity. VIF greater than 5 identified possible collinearity between predictors. None of the identified predictors had VIF greater than 5, which suggests no collinearity of predictors. Pearson goodness-of-fit was used to assess the multivariable model fit and was not significant at the 5% level ($P = 0.127$), thus the multivariable model could not be rejected. STATA v14.0-MP (StataCorp LLC) was used for all data analysis.

Results

There were an estimated 5,559,395 discharges between 1998 and 2013, with procedure codes for a CABG, valve repair or replacement, or left ventricular assist device (fig. 1). A diagnosis of ION was documented in 794 of those procedures, corresponding to an average yearly incidence of 1.43 per 10,000 cardiac surgeries (95% CI, 1.23 to 1.67; table 1). After adjusting for changes in procedural volume, there was no significant change in the yearly incidence of ION in cardiac surgery (OR, 1.01; $P = 0.574$; fig. 2). There were an estimated 9,520,478 discharges with procedure codes for PCI, and 206 had a diagnosis for ION (see Supplemental Digital Content 2, Figure, http://links.lww.com/ALN/B375, which illustrates the incidence of ION in PCI). The incidence of ION in PCI was 0.22 per 10,000 (95% CI, 0.16 to 0.30), significantly less than that for patients undergoing isolated CABG ($P = 0.0001$).

Isolated CABG surgery accounted for the highest volume of diagnoses of ION (621 of 794; 78%), followed by a combined CABG and valve repair or replacement (86 of 794; 11%), valve repair or replacement alone (78 of 794; 10%), and left ventricular assist device (10 of 794; 1.3%). The incidence of ION for each procedure category is illustrated in figure 1. The incidence of ION was not different between the different cardiac surgery procedures ($P = 0.0596$).

Figure 3 shows changes in cardiac surgery procedures from 1998 to 2013. There was a 60% decrease in CABG as the sole procedure from 1998 to 2013 (1,725 to 686 per million adults), 1,092% increase in left ventricular assist device (1.3 to 14.2 per million), 53% increase in valve repair or replacement alone (206 to 315 per million), and a 22% decrease in combined CABG and valve repair or replacement (176 to 137 per million; $P = 0.0001$).

Characteristics of patients with a cardiac surgical procedure are presented in table 2, and characteristics of patients with a PCI are presented in the Table, Supplemental Digital Content 3, http://links.lww.com/ALN/B376.

A univariable analysis was performed for all cardiac surgery patient characteristics and for primary and secondary cardiac procedures (table 2). Significant characteristics and procedures from the univariable analysis ($P < 0.20$) were combined to create a multivariable logistic regression (table 3). Patient characteristics, from the multivariable model, associated with increased odds of ION include carotid artery stenosis (OR, 2.70; 95% CI, 1.52 to 4.80; $P = 0.001$), stroke (OR, 3.43; 95% CI, 1.73 to 6.80; $P = 0.0004$), diabetic retinopathy (OR, 3.83; 95% CI, 1.84 to 7.95; $P = 0.0003$), hypertensive retinopathy (OR, 30.09; 95% CI, 6.21 to 145.64; $P = 0.0001$), glaucoma (OR, 2.68; 95% CI, 1.04 to

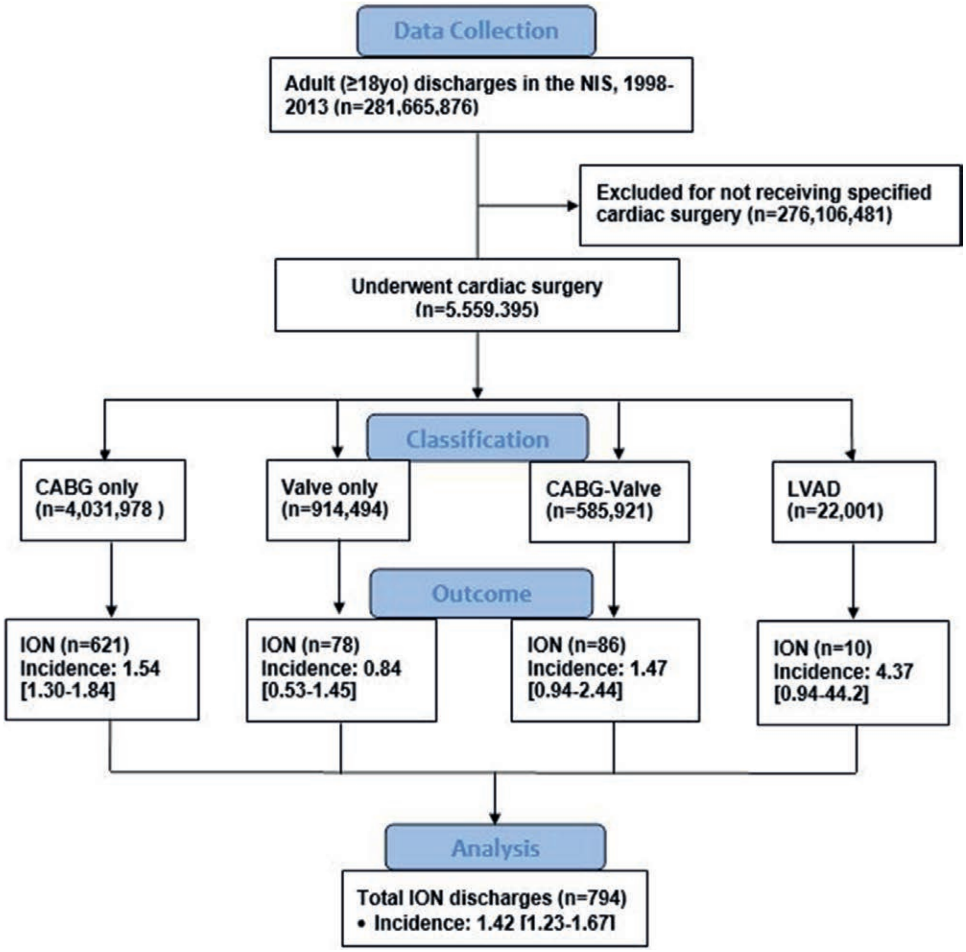


Fig. 1. Consolidated Standards of Reporting Trials (CONSORT) diagram of ischemic optic neuropathy (ION) in cardiac surgery. Data collection was through patient discharges recorded in the National Inpatient Sample (NIS) from 1998 to 2013. Only patients aged 18 yr or older who underwent a specified cardiac procedure (coronary artery bypass graft [CABG] only, valve repair or replacement only, CABG valve repair or replacement as a combined procedure, or left ventricular assist device [LVAD]) were included in the analysis, and all other patients were excluded. The primary outcome, ION, was reported as volume (n) and incidence per 10,000 (95% CI). Results are nationwide estimates using NIS weighting and STATA (StataCorp LLC) survey function. CABG only = only received coronary artery bypass graft; CABG valve = received both coronary artery bypass graft and cardiac valve repair or replacement; Valve only = only received cardiac valve repair or replacement.

6.93; P = 0.042), age-related macular degeneration (OR, 4.50; 95% CI, 1.13 to 17.87; P = 0.032), and cataract (OR, 5.62; 95% CI, 1.71 to 18.45; P = 0.004; fig. 4A). Female sex (OR, 0.59; 95% CI, 0.38 to 0.92; P = 0.019) and uncomplicated diabetes mellitus type 2 (OR, 0.51; 95% CI, 0.32 to 0.83; P = 0.006) were associated with lower ORs (fig. 4B). The primary procedures associated with increased odds of ION were left ventricular assist device (OR, 13.82; 95% CI, 1.75 to 109.01; P = 0.013) and two-vessel CABG (OR, 1.78; 95% CI, 1.04 to 3.06; P = 0.035; fig. 4A). CPB was not associated with increased odds of ION (OR, 0.78; P = 0.219).

Discussion

The incidence of ION in CABG, valve repair or replacement, and left ventricular assist device, from 1998 to 2013, was 1.43 per 10,000 with no significant trend over the study period. The estimated incidence of ION after PCI, in the same database, was 0.22 per 10,000, near the lower end of previous national estimates of ION incidence in the general adult population at 2 to 10 per 100,000.[24,25] The seven-fold higher incidence of ION in cardiac surgery as compared to PCI and previous national estimates supports previous studies identifying cardiac surgery as high risk for developing ION and suggests that our findings are due to the development of ION during the perioperative period, and not due to a preexistent diagnosis. Overall, no differences in the incidence of ION were identified between the different cardiac surgeries; however, in the multivariable analysis, left ventricular assist device and two-vessel CABG were associated with increased odds of ION. Two-vessel CABG accounted for the highest percentage of isolated CABG procedures and diagnoses of ION; although this was accounted for in the multivariable analysis. It should be

Table 1. National Estimates of ION in Cardiac Surgery Cases in the National Inpatient Sample, 1998–2013

Year	Cardiac Cases (95% CI)	ION (95% CI)	ION Incidence (per 10,000; 95% CI)
1998	422,329 (372,256–472,401)	65 (27–103)	1.54 (0.91–2.84)
1999	399,492 (344,505–454,480)	96 (45–147)	2.41 (1.58–3.88)
2000	429,030 (381,780–476,281)	68 (26–110)	1.58 (0.95–2.83)
2001	434,215 (385,513–482,916)	41 (11–70)	0.93 (0.48–2.10)
2002	406,079 (357,699–454,459)	68 (15–121)	1.68 (1.03–2.94)
2003	392,455 (347,906–437,004)	28 (3–54)	0.73 (0.33–1.92)
2004	348,837 (313,534–384,140)	42 (12–73)	1.21 (0.64–2.58)
2005	325,036 (286,843–363,230)	34 (7–60)	1.04 (0.51–2.51)
2006	353,147 (311,112–395,181)	53 (19–86)	1.49 (0.84–2.91)
2007	297,131 (266,279–327,982)	19 (0–40)	0.65 (0.24–2.35)
2008	312,092 (281,506–342,678)	29 (7–51)	0.93 (0.42–2.45)
2009	331,771 (288,738–374,804)	53 (17–89)	1.65 (0.95–3.13)
2010	271,885 (245,556–298,154)	24 (2–47)	0.90 (0.38–2.69)
2011	278,957 (245,296–312,619)	19 (0–38)	0.67 (0.25–2.43)
2012	277,570 (262,438–292,703)	80 (37–123)	2.88 (1.80–4.94)
2013	279,400 (264,082–294,718)	75 (34–116)	2.68 (1.65–4.69)
Total	5,559,395 (5,194,174–5,924,617)	794 (638–951)	1.43 (1.23–1.67)

To calculate incidence of ischemic optic neuropathy per 10,000 yearly estimates of ION was divided by yearly estimates of cardiac surgical procedures. Estimates from the National Inpatient Sample were created using the trend weights and stratum variables from the National Inpatient Sample and the survey function of STATA (StataCorp LLC). Cardiac cases include coronary artery bypass grafts only, coronary artery bypass graft with valve repair or replacement, valve repair or replacement only, and left ventricular assist device insertion.

ION = ischemic optic neuropathy.

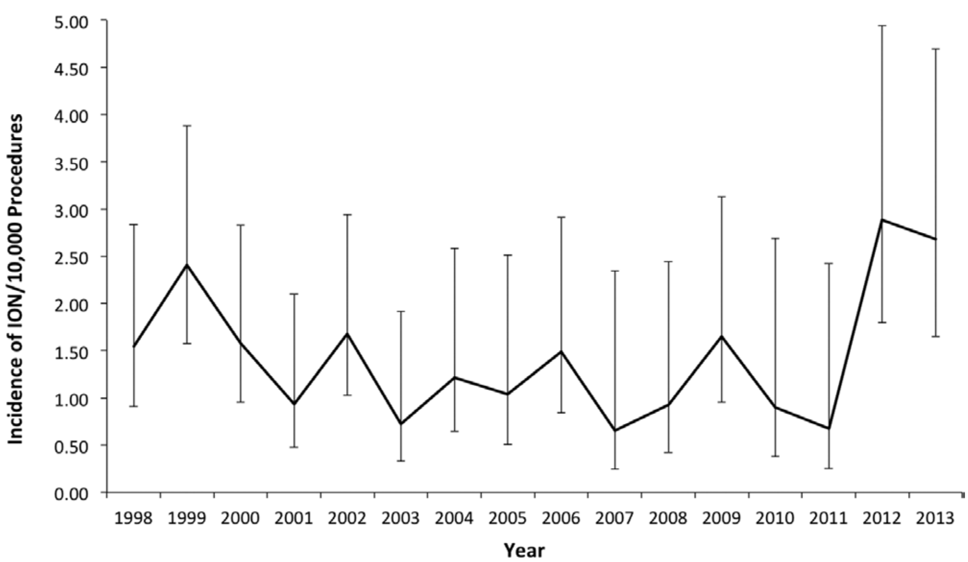


Fig. 2. Ischemic optic neuropathy (ION) incidence in cardiac surgery cases in the National Inpatient Sample (NIS), 1998 to 2013. Results are nationwide estimates using NIS weighting and STATA (StataCorp LLC) survey function. After adjusting for changes in procedural volume in the multivariable analysis, there was no significant change in yearly incidence of ION (odds ratio, 1.01, $P = 0.574$). Cardiac surgery cases include coronary artery bypass grafts only, coronary artery bypass graft with valve repair or replacement, valve repair or replacement only, and left ventricular assist device insertion. To calculate incidence of ION per 10,000, yearly estimates of ION were divided by yearly estimates of cardiac surgical procedures. *Error bars* are 95% CIs.

noted that left ventricular assist device procedural volume was smaller relative to the other cardiac surgeries, which led to wide 95% CIs for the estimate, thus the result should be interpreted cautiously.

Carotid artery stenosis and stroke were associated with increased risk of ION in our study. Carotid artery stenosis has been listed in numerous case reports as a diagnosis in affected patients, and atherosclerosis was previously identified in a single-center retrospective cohort as a risk factor.[2,9,26,27] However, neither stroke nor carotid stenosis has been identified as a risk factor for spontaneously (nonperioperative) occurring ION.[28,29] Taken together, these findings suggest that in cardiac surgery, hypotension, systemic inflammation, or other as yet unknown perioperative mechanisms may interact with already decreased perfusion *via* the carotid circulation to heighten the risk of ION.

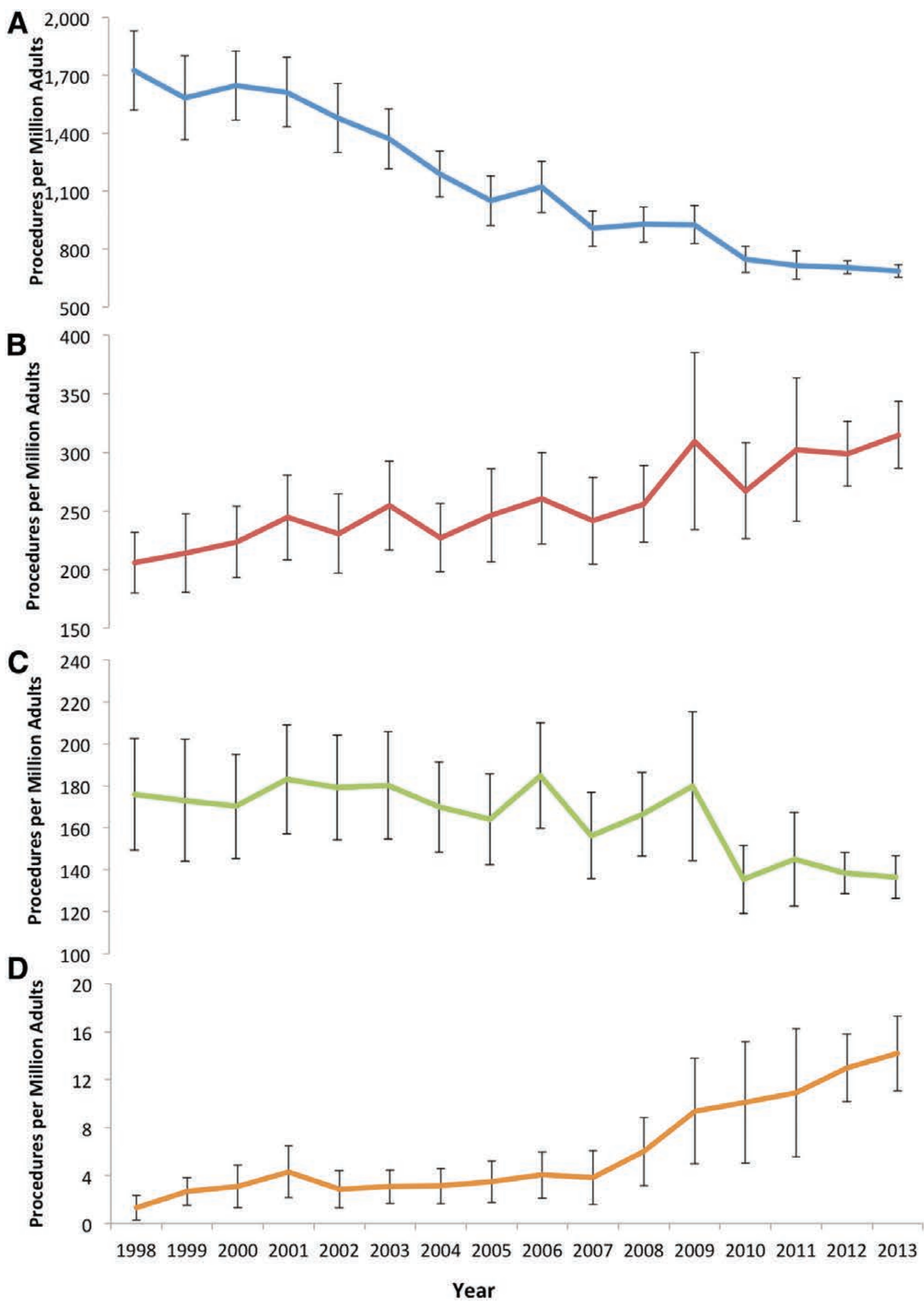


Fig. 3. Yearly volume of cardiac procedures in the National Inpatient Sample (NIS) per 1 million U.S. adult population from 1998 to 2013. To calculate incidence of cardiac procedures per 1 million, yearly estimates of each procedure type were divided by the yearly U.S. population estimate based on U.S. Census Bureau data (http://www.census.gov/popest/data/historical/index.html). Results are nationwide estimates using NIS weighting and STATA (StataCorp LLC) survey function. There was a 60% decrease in coronary artery bypass graft (CABG) as the sole procedure from 1998 to 2013 (1,725 to 686 per million adults), 1,092% increase in left ventricular assist device (LVAD; 1.3 to 14.2 per million), 53% increase in valve replacement alone (206 to 315 per million), and a 22% decrease in combined CABG valve (176 to 137 per million; $P = 0.0001$). Cardiac procedure types include (*A*) CABG only, (*B*) valve repair or replacement only (Valve only), (*C*) CABG valve repair or replacement (CABG-Valve), and (*D*) LVAD. *Error bars* are 95% CIs.

Our study identified chronic eye conditions associated with altered posterior eye circulation such as glaucoma, age-related macular degeneration, diabetic retinopathy, and hypertensive retinopathy as risk factors in perioperative ION. Glaucoma and age-related macular degeneration may predispose the optic nerve to ischemia due to impaired autoregulation of blood flow.[30–32] Similarly, diabetic retinopathy and hypertensive retinopathy are characterized with

Table 2. Characteristics and Univariable Analysis of All Cardiac Surgery Cases with and without Ischemic Optic Neuropathy in the National Inpatient Sample, 1998 to 2013

Cases	All Cases: ION	All Cases: Unaffected	Odds Ratio	*P* Value
All patients: no. of discharges	794	5,558,601		
Mean length of stay days (95% CI)	12.0 (10.1–13.8)	10.1 (10.0–10.3)	1.004	0.0001
Mean total charges, $ (95% CI; inflation adjusted to 2013)	123,539 (103,723–143,354)	129,556 (125,179–133,932)	1.00	0.586
Type of admission, %				
Elective	254 (32.0)	1,993,517 (35.9)		
Nonelective	271 (34.1)	1,872,802 (33.7)		
Missing	270 (34.0)	1,692,282 (30.4)		
Discharge status, %				
Routine	355 (44.7)	2,776,293 (49.9)	Ref	—
Short-term hospital	< 10 (< 1.3)	46,826 (0.8)	0.79	0.823
Home health care	287 (36.1)	1,606,369 (28.9)	1.40	0.066
Other	144 (18.1)	934,923 (16.8)	1.21	0.385
Died	< 10 (< 1.3)	186,874 (3.4)	0.20	0.117
Missing	< 10 (1.3)	7,316 (0.1)	1.0	—
Race, %				
White	561 (70.7)	3,515,288 (63.2)		
Black	30 (3.8)	266,398 (4.8)		
Hispanic	< 10 (< 1.3)	270,530 (4.9)		
Asian or Pacific Islander	< 10 (< 1.3)	87,460 (1.6)		
Native American	< 10 (< 1.3)	18,738 (0.3)		
Other	24 (3.0)	138,925 (2.5)		
Missing	170 (21.4)	1,261,263 (22.7)		
CABG only, %				
One vessel	77 (12.4)	574,363 (14.2)	Ref	—
Two vessels	272 (43.8)	2,353,560 (58.4)	1.75	0.032
Three vessels	181 (29.1)	1,259,978 (31.3)	1.20	0.473
Four vessels	81 (13.0)	659,428 (16.4)	1.02	0.940
Unspecified no. of vessels	10 (1.6)	184,029 (4.6)	0.52	0.311
Total CABG only	621 (78.2)	4,031,357 (72.5)	1.35	0.143
Valve only,* %	78 (9.8)	919,417 (16.5)	0.55	0.027
CABG and valve,† %	86 (10.8)	585,836 (10.5)	1.03	0.899
LVAD, %	10 (1.3)	21,991 (0.40)	3.09	0.129
Intraaortic balloon pump, %	54 (6.8)	447,182 (8.0)	0.83	0.562
Cardiopulmonary bypass, %	597	4,436,073	0.76	0.151
Age group, yr, %				
< 57	226 (28.5)	1,378,470 (24.8)	Ref	—
57–65	193 (24.3)	1,183,066 (21.3)	1.00	0.982
66–74	220 (27.7)	1,612,801 (29.0)	0.83	0.409
> 75	155 (19.5)	1,384,265 (24.9)	0.68	0.105
Sex, %				
Female	189 (23.8)	1,771,498 (31.9)	0.67	0.033
Male	605 (76.1)	3,786,443 (68.1)	Ref	—
Obesity, %	108 (13.6)	621,890 (11.2)	1.25	0.329
Obstructive sleep apnea, %	24 (3.0)	145,126 (2.6)	1.19	0.718
Hyperlipidemia, %	432 (54.4)	2,668,295 (48.0)	1.29	0.123
Smoking, %	197 (24.8)	1,495,130 (26.9)	0.89	0.572
Hypertension, %	549 (69.1)	3,630,926 (65.3)	1.19	0.319
DM type 1 without complications, %	15 (1.9)	93,954 (1.7)	0.09	0.879
DM type 2 without complications, %	113 (14.2)	1,364,385 (24.5)	0.51	0.004
Diabetic retinopathy, %	48 (6.0)	67,719 (1.2)	5.21	0.001
DM with renal manifestations, %	20 (6.0)	72,524 (1.3)	1.92	0.216
DM with neurologic manifestations, %	24 (3.0)	104,678 (1.9)	1.65	0.288
DM with peripheral circulatory disorders, %	< 10 (< 1.3)	17,637 (0.3)	1.0	—
Peripheral vascular disease, %	72 (9.1)	279,146 (5.0)	1.90	0.020
Coronary artery disease, %	714 (89.9)	4,731,611 (85.1)	1.55	0.132

(*Continued*)

Table 2. (Continued)

Cases	All Cases: ION	All Cases: Unaffected	Odds Ratio	*P* Value
Carotid artery stenosis, %	77 (9.7)	204,815 (3.7)	2.82	0.001
Stroke, %	44 (5.5)	120,700 (2.2)	2.62	0.005
Atrial fibrillation, %	197 (24.8)	1,696,490 (30.5)	0.75	0.139
Congestive heart failure, %	139 (17.5)	1,306,558 (23.5)	0.69	0.108
Cardiogenic shock, %	30 (3.8)	180,784 (3.3)	1.15	0.729
Pulmonary hypertension, %	39 (4.9)	282,533 (5.1)	0.97	0.936
Anemia, %	267 (33.6)	1,745,545 (31.4)	1.11	0.555
Blood transfusion, %	184 (23.2)	1,272,784 (22.9)	1.01	0.941
Acute kidney injury, %	55 (6.9)	539,574 (9.7)	0.69	0.261
Chronic kidney disease, %	30 (3.8)	279,727 (5.0)	0.73	0.472
Glaucoma, %	28 (3.5)	65,253 (1.2)	3.08	0.009
Age-related macular degeneration, %	11 (1.4)	17,744 (0.3)	4.29	0.046
Hypertensive retinopathy, %	< 10 (< 1.3)	1,502 (0.03)	46.44	0.001
Cataract, %	21 (2.6)	15,643 (0.3)	9.46	0.001

Results are nationwide estimates using National Inpatient Sample weighting and STATA (StataCorp LLC) survey function. Numbers are presented as count estimates or means with percent in parentheses and respective 95% CIs in parentheses when indicated. Results with n < 10 could not be reported due to Agency for Healthcare Research and Quality regulations. See table, Supplemental Digital Content 1, http://links.lww.com/ALN/B374, for International Classification of Diseases, Ninth Revision–Clinical Modification diagnostic codes used to identify noted characteristics. Total charges were inflation adjusted to 2013 dollars using Bureau of Labor Statistics (http://www.bls.gov/data/). Cardiac cases include procedures with only coronary artery bypass grafts, coronary artery bypass grafts with valve repair or replacement, only cardiac valve repair or replacements, and left ventricular assist device insertions.

*Valve only indicates only cardiac valve repair or replacements. †CABG and valve indicates CABG with valve repair or replacement.

CABG = coronary artery bypass grafts; DM = diabetes mellitus; ION = ischemic optic neuropathy; LVAD = left ventricular assist device; Ref = Reference category.

endothelial damage, a leaky blood–retinal barrier, vascular occlusion, and ischemia, leading to neovascularization.[33] Development of ION may be associated with these conditions due to impaired microcirculation diffusely within the eye including the optic nerve. Thus, these degenerative eye conditions could be a marker of more widespread ocular circulatory abnormalities.[34] A 2014 analysis of posterior spine fusion surgery in the NIS found an increased risk of visual loss in patients with diabetes with end-organ damage, but the association with ION is unclear as the study included discharges with cortical blindness, and retinal artery occlusion in addition to ION.[35]

These chronic degenerative eye conditions may be markers of increased risk of ION after cardiac surgery, but the results should be interpreted cautiously. Patients who developed perioperative ION likely underwent a detailed ophthalmologic exam to confirm the diagnosis leading to a heightened diagnosis intensity of degenerative eye conditions.[36] Increased diagnosis intensity may have led to the association seen between ION and cataract, as there is no theoretical reason for its association. In contrast, glaucoma requires multiple exams and more sophisticated technology for a diagnosis, and an initial diagnosis was unlikely to occur during the hospital admission for cardiac surgery.[37]

Female sex and uncomplicated diabetes were associated with a decrease in the odds of ION after cardiac surgery. The female visual pathway is not known to anatomically differ *versus* the male visual pathway; however, hormonal factors such as estrogen may play a role. Estrogen improves vascular function and decreases atherosclerosis; however, female sex had decreased odds of ION in our study even when controlling for vascular disease and carotid artery stenosis in the multivariable regression leaving the mechanism for this decrease unclear.[38,39] The reason why ION risk in this study differed between uncomplicated diabetes mellitus type 2 and diabetic retinopathy is not known and will require further study.

ION was not associated with factors specific to cardiac surgery that may decrease optic nerve blood flow or embolic events, including CPB, cardiogenic shock, congestive heart failure, atrial fibrillation, pulmonary hypertension, and anemia.[1,2,4] Several case series and case reports of ION after cardiac surgery identified anemia, blood loss, and lowest hemoglobin level as possible risk factors for ION; however, we did not find anemia or transfusion as significant risk factors. Kalyani *et al.*[4] found a trend toward a perioperative change in hemoglobin levels and risk of ION but not a significant association. Nuttall *et al.*[2] and Shapira *et al.*[1] identified low postoperative hemoglobin concentrations as an independent risk factor for ION in cardiac surgery after CPB. In the NIS, these data may not accurately reflect perioperative hemoglobin values.

Our study has limitations secondary to using an administrative database. The NIS is a stratified probability sample of inpatient discharges and hospitals in the sampling frame of all nonfederal hospitals in the United States. As such, because ION is a rare event, oversampling or overweighting of discharges containing a diagnosis of ION may have increased the incidence of ION. However, the NIS is a robust 20% sample of the entire NIS universe and has been rigorously validated.[40] Discharge records are susceptible to ICD-9-CM coding errors for a diagnosis of ION. The incidence of ION

Table 3. Multivariable Analysis for Ischemic Optic Neuropathy for Cardiac Surgery Cases in the National Inpatient Sample, 1998 to 2013

	Odds Ratio	95% CI	*P* Value
Year	1.01	0.97–1.06	0.574
Age group, yr			
< 57		Reference	
57–65	0.94	0.60–1.48	0.806
66–74	0.77	0.48–1.24	0.286
> 75	0.64	0.37–1.10	0.106
Sex			
Male		Reference	
Female	0.59	0.38–0.92	0.019
Hyperlipidemia	1.16	0.81–1.67	0.425
DM type 2 without complications*	0.51	0.32–0.83	0.006
Diabetic retinopathy	3.83	1.84–7.95	0.0003
Peripheral vascular disease	1.44	0.80–2.59	0.222
Carotid artery stenosis	2.70	1.52–4.80	0.001
Stroke	3.43	1.73–6.80	0.0004
Atrial fibrillation	0.84	0.55–1.28	0.417
Congestive heart failure	0.77	0.47–1.26	0.297
Glaucoma	2.68	1.04–6.93	0.042
Age-related macular degeneration	4.50	1.13–17.87	0.032
Hypertensive retinopathy	30.09	6.21–145.84	0.0001
Cataract	5.62	1.71–18.45	0.004
CABG			
One vessel		Reference	
Two vessels	1.78	1.04–3.06	0.035
Three vessels	1.23	0.72–2.09	0.445
Four vessels	1.04	0.53–2.06	0.903
Unspecified no. of grafts	0.50	0.14–1.79	0.288
Valve†	1.25	0.70–2.25	0.447
LVAD	13.82	1.75–109.01	0.013
Cardiopulmonary bypass	0.78	0.52–1.16	0.219

Stroke, carotid artery stenosis, glaucoma, age-related macular degeneration, diabetic and hypertensive retinopathy, cataract, left ventricular assist device, and two-vessel coronary artery bypass graft were associated with increased risk of postoperative ischemic optic neuropathy. Female gender and uncomplicated diabetes type II were associated with a decreased risk of postoperative ischemic optic neuropathy. Results are nationwide estimates using National Inpatient Sample weighting and STATA (StataCorp LLC) survey function. A multivariate logistic regression was performed including all patient characteristics and procedures that were significant ($P < 0.20$) in the univariate analysis. In the multivariable analysis, $P \leq 0.05$ was used to identify significant risk factors. Results are reported as odds ratios with 95% CIs. Cardiac cases include coronary artery bypass grafts, coronary artery bypass grafts with valve repair or replacement, cardiac valve repair or replacements, and left ventricular assist device insertions.

*Without ophthalmic, renal, neurologic, or peripheral circulatory complications. †Valve indicates valve repair or replacement.

CABG = coronary artery bypass graft; DM = diabetes mellitus; LVAD = left ventricular assist device; Reference = reference category.

is low, and small errors in diagnostic coding could have a large impact on our findings. However, our unweighted sample size is greater than 1 million admissions, which mitigates systematic reporting bias, and previous studies have used the NIS to identify the incidence of ION in various surgical populations.[8]

Our study is limited to identifying patient conditions and surgical procedures associated with increased odds of ION after cardiac surgery. As such, patient conditions reported in the NIS using ICD-9-CM codes may not accurately reflect the clinical spectrum of severity, such as in cardiogenic shock or anemia. Thus, while our study did not find a diagnosis of anemia to be a significant risk factor for developing ION, it is possible that the lack of granularity may have impacted our results. Furthermore, the NIS does not contain any intraoperative information about the anesthetic or intraoperative care such as duration of CPB. Additionally, ICD-9-CM codes do not exist for certain aspects of the procedure such as redo sternotomy, which may impact the development of ION.

The temporal relationship between a diagnosis of ION and the timing of the cardiac surgery cannot be determined in the NIS, thus the cardiac surgery population may have had a higher baseline prevalence of ION. However, the seven-fold higher incidence of ION after CABG as compared to PCI and previous national estimates strongly suggests that the majority of ION we observed occurred after cardiac surgery. The severity of visual loss cannot be determined from the database as well as longitudinal follow-up for progression or improvement after discharge. The NIS represents a single inpatient admission and does not contain any patient identifiers to allow patients to be identified for follow-up.

In conclusion, cardiac surgery has an incidence of perioperative ION with an average yearly incidence of 1.43 per 10,000 procedures; the majority of the cases were associated with isolated CABG. This incidence was about seven times that of a comparable inpatient group undergoing percutaneous cardiac intervention, as well as the known incidence of spontaneously occurring ION in the general population. The yearly incidence has not changed despite decreases in CABG, increases in left ventricular assist device, and an overall decrease in cardiac surgery volume between 1998 and 2013. ION is most frequently associated with carotid artery stenosis, stroke, male sex, degenerative eye conditions, two-vessel CABG, and left ventricular assist device. Uncomplicated diabetes type 2 and female sex were associated with a lower risk of ION. Further research is needed to identify potential therapeutic interventions to decrease the risk of this rare and devastating complication.

Acknowledgments

The authors are grateful to Ms. Chuanhong Liao, M.S., Senior Biostatistician, Department of Public Health Sciences, University of Chicago, Chicago, Illinois, for assistance with the statistical analysis.

Research Support

Supported by the following grants from the National Institutes of Health (Bethesda, Maryland): RO1 EY10343, to Dr. Roth; UL1 RR024999, to the University of Chicago Institute for Translational Medicine (Chicago, Illinois); UL1 TR002003, to the University of Illinois at Chicago

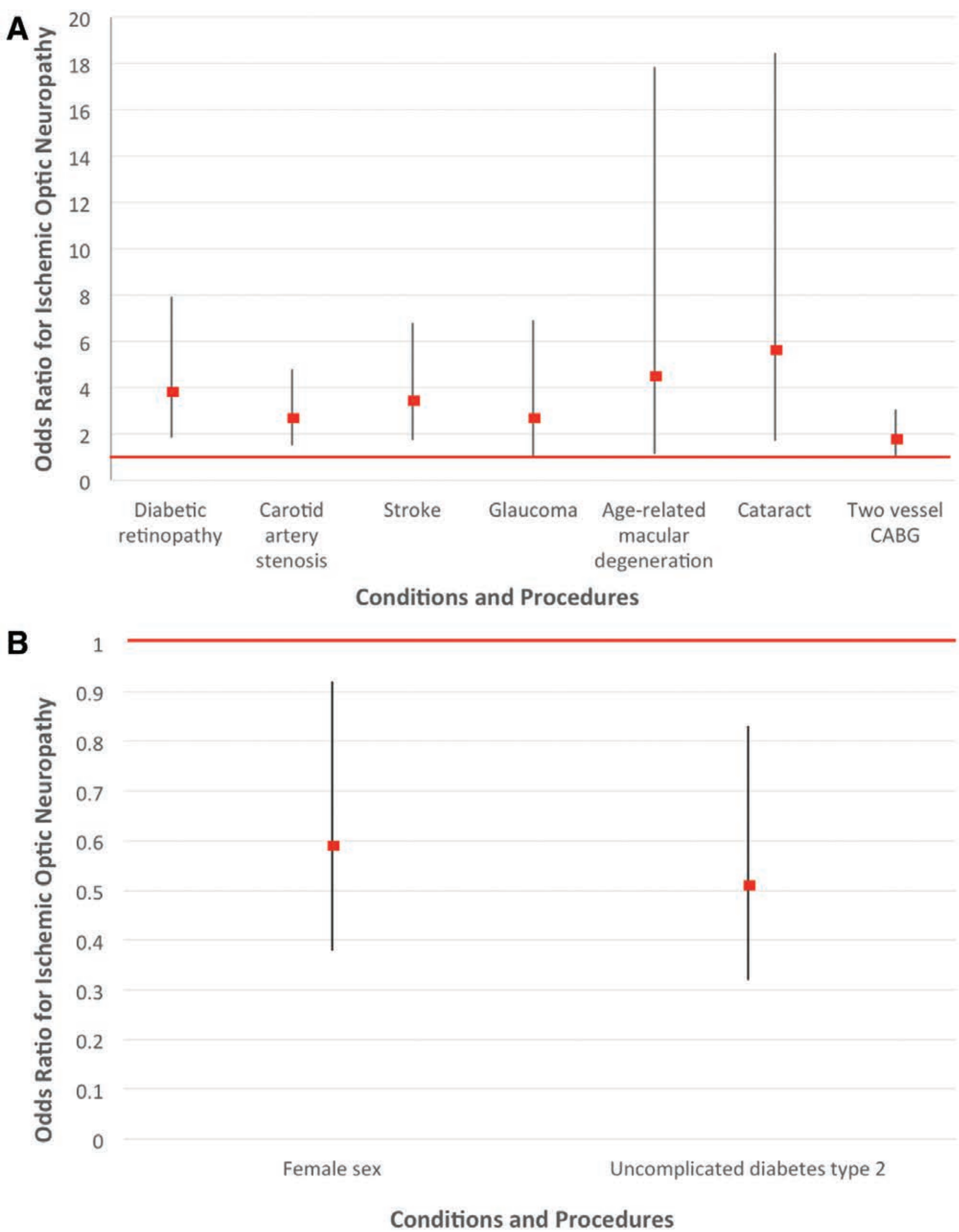


Fig. 4. Odds ratios for conditions that increase and decrease odds of ischemic optic neuropathy (ION) in cardiac surgery. Odds ratios from the multivariable analysis for patient conditions that increase and decrease odds of developing perioperative ION after cardiac surgery. (*A*) Conditions and procedures that increase odds of developing ION (odds ratio and 95% CIs). Of note, hypertensive retinopathy and left ventricular assist device procedure were left off of the graph secondary to large CIs. (*B*) Conditions that decrease odds of developing ION after cardiac surgery (odds ratios and 95% CIs).

Center for Clinical and Translational Science (Chicago, Illinois); and K23 EY024345, to Dr. Moss. Also supported by core grant No. P30 EY001792 from the Department of Ophthalmology and Visual Sciences of the University of Illinois, the University of Chicago Pritzker School of Medicine Summer Research Program (Chicago, Illinois; to Ms. Matsumoto), and an unrestricted grant from Research to Prevent Blindness (New York, New York; to Dr. Moss, Dr. Joslin, and Dr. Roth) and from the Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago (Chicago, Illinois; to Dr. Moss, Dr. Joslin, and Dr. Roth).

Competing Interests

Dr. Roth has served as an expert witness in cases of perioperative eye injuries on behalf of patients, physicians, and hospitals. The other authors declare no competing interests.

Correspondence

Address correspondence to Dr. Rubin: Department of Anesthesia and Critical Care, University of Chicago Medicine, 5841 South Maryland, Box M.C. 4028, Chicago, Illinois 60637. drubin@dacc.uchicago.edu. Information on purchasing reprints may be found at www.anesthesiology.org or on

the masthead page at the beginning of this issue. Anesthesiology's articles are made freely accessible to all readers, for personal use only, 6 months from the cover date of the issue.

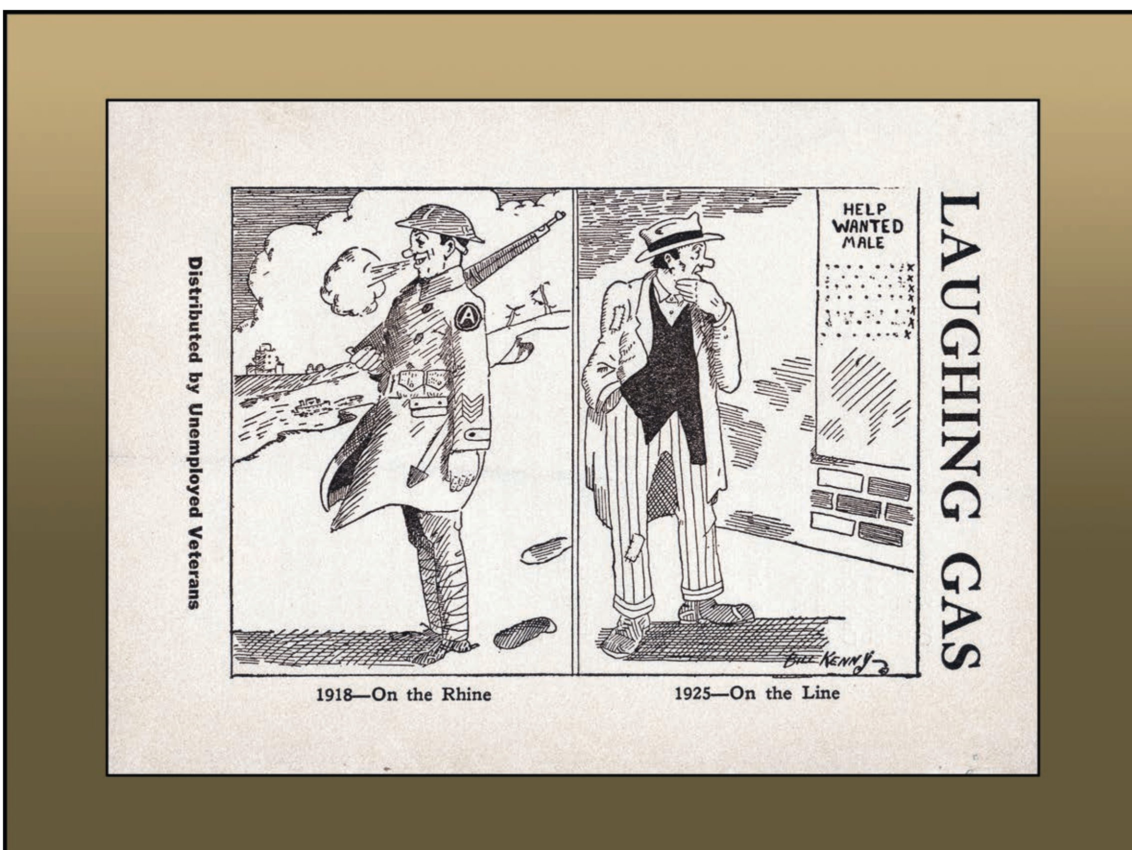
References

1. Shapira OM, Kimmel WA, Lindsey PS, Shahian DM: Anterior ischemic optic neuropathy after open heart operations. Ann Thorac Surg 1996; 61:660–6
2. Nuttall GA, Garrity JA, Dearani JA, Abel MD, Schroeder DR, Mullany CJ: Risk factors for ischemic optic neuropathy after cardiopulmonary bypass: A matched case/control study. Anesth Analg 2001; 93:1410–6, table of contents
3. Shen Y, Drum M, Roth S: The prevalence of perioperative visual loss in the United States: A 10-year study from 1996 to 2005 of spinal, orthopedic, cardiac, and general surgery. Anesth Analg 2009; 109:1534–45
4. Kalyani SD, Miller NR, Dong LM, Baumgartner WA, Alejo DE, Gilbert TB: Incidence of and risk factors for perioperative optic neuropathy after cardiac surgery. Ann Thorac Surg 2004; 78:34–7
5. Postoperative Visual Loss Study Group: Risk factors associated with ischemic optic neuropathy after spinal fusion surgery. Anesthesiology 2012; 116: 15–24
6. American Society of Anesthesiologists Task Force on Perioperative Visual Loss: Practice advisory for perioperative visual loss associated with spine surgery: An updated report by the American Society of Anesthesiologists Task Force on Perioperative Visual Loss. Anesthesiology 2012; 116: 274–85
7. Patil CG, Lad EM, Lad SP, Ho C, Boakye M: Visual loss after spine surgery: A population-based study. Spine (Phila Pa 1976) 2008; 33:1491–6
8. Rubin DS, Parakati I, Lee LA, Moss HE, Joslin CE, Roth S: Perioperative visual loss in spine fusion surgery: Ischemic optic neuropathy in the United States from 1998 to 2012 in the Nationwide Inpatient Sample. Anesthesiology 2016; 125:457–64
9. Sweeney PJ, Breuer AC, Selhorst JB, Waybright EA, Furlan AJ, Lederman RJ, Hanson MR, Tomsak R: Ischemic optic neuropathy: A complication of cardiopulmonary bypass surgery. Neurology 1982; 32:560–2
10. Kim LK, Looser P, Swaminathan RV, Minutello RM, Wong SC, Girardi L, Feldman DN: Outcomes in patients undergoing coronary artery bypass graft surgery in the United States based on hospital volume, 2007 to 2011. J Thorac Cardiovasc Surg 2016; 151: 1686–92
11. Shah N, Agarwal V, Patel N, Deshmukh A, Chothani A, Garg J, Badheka A, Martinez M, Islam N, Freudenberger R: National trends in utilization, mortality, complications, and cost of care after left ventricular assist device implantation from 2005 to 2011. Ann Thorac Surg 2016; 101:1477–84
12. Bojikian KD, Chen CL, Wen JC, Zhang Q, Xin C, Gupta D, Mudumbai RC, Johnstone MA, Wang RK, Chen PP: Optic disc perfusion in primary open angle and normal tension glaucoma eyes using optical coherence tomography-based microangiography. PLoS One 2016; 11:e0154691
13. Harris A, Chung HS, Ciulla TA, Kagemann L: Progress in measurement of ocular blood flow and relevance to our understanding of glaucoma and age-related macular degeneration. Prog Retin Eye Res 1999; 18:669–87
14. Gálvez-Ruiz A, Schatz P: Prevalence of diabetic retinopathy in a population of diabetics from the Middle East with microvascular ocular motor palsies. J Neuroophthalmol 2016; 36:131–3
15. Moss HE: Retinal vascular changes are a marker for cerebral vascular diseases. Curr Neurol Neurosci Rep 2015; 15:40
16. Agency for Healthcare Research and Quality: Overview of The National Inpatient Sample (NIS). Rockville, Maryland, Healthcare Cost and Utilization Project (HCUP), 2016
17. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Available at: http://www.cdc.gov/nchs/icd/icd9cm.htm. Updated June 18, 2013. Accessed June 15, 2016
18. US Department of Labor. Bureau of Labor Statistics. Consumer Price Index. Available at: https://www.bls.gov/. Updated May 2016. Accessed June 10, 2016
19. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative: Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. BMJ 2007; 335:806–8
20. Kuriyan AE, Lam BL: Non-arteritic anterior ischemic optic neuropathy secondary to acute primary-angle closure. Clin Ophthalmol 2013; 7:1233–8
21. Reddy D, Rani PK, Jalali S, Rao HL: A study of prevalence and risk factors of diabetic retinopathy in patients with non-arteritic anterior ischemic optic neuropathy (NA-AION). Semin Ophthalmol 2015; 30:101–4
22. Koch GG FD, Freeman JL: Strategies in the multivariate analysis of data from complex surveys. International Statistical Review 1975; 43: 59–78
23. US Census Bureau. Population estimates. Available at: https://www.census.gov/popest. Updated June 23, 2016. Accessed July 1, 2016
24. Johnson LN, Arnold AC: Incidence of nonarteritic and arteritic anterior ischemic optic neuropathy: Population-based study in the state of Missouri and Los Angeles County, California. J Neuroophthalmol 1994; 14:38–44
25. Hattenhauer MG, Leavitt JA, Hodge DO, Grill R, Gray DT: Incidence of nonarteritic anterior ischemic optic neuropathy. Am J Ophthalmol 1997; 123:103–7
26. Moster ML: Visual loss after coronary artery bypass surgery. Surv Ophthalmol 1998; 42:453–7
27. Williams EL, Hart WM Jr, Tempelhoff R: Postoperative ischemic optic neuropathy. Anesth Analg 1995; 80:1018–29
28. Jacobson DM, Vierkant RA, Belongia EA: Nonarteritic anterior ischemic optic neuropathy: A case-control study of potential risk factors. Arch Ophthalmol 1997; 115:1403–7
29. Lee MS, Grossman D, Arnold AC, Sloan FA: Incidence of nonarteritic anterior ischemic optic neuropathy: Increased risk among diabetic patients. Ophthalmology 2011; 118:959–63
30. Sakata R, Aihara M, Murata H, Mayama C, Tomidokoro A, Iwase A, Araie M: Contributing factors for progression of visual field loss in normal-tension glaucoma patients with medical treatment. J Glaucoma 2013; 22:250–4
31. Ohtake H, Misaki T, Matsunaga Y, Tubota M, Watanabe Y, Shirao Y: Open heart surgery under total extracorporeal circulation in a patient with advanced glaucoma. Cardiovasc Surg 1993; 1:190–1
32. Ciulla TA, Harris A, Kagemann L, Danis RP, Pratt LM, Chung HS, Weinberger D, Garzozi HJ: Choroidal perfusion perturbations in non-neovascular age related macular degeneration. Br J Ophthalmol 2002; 86:209–13
33. Fleming AD, Goatman KA, Philip S, Williams GJ, Prescott GJ, Scotland GS, McNamee P, Leese GP, Wykes WN, Sharp PF, Olson JA; Scottish Diabetic Retinopathy Clinical Research Network: The role of haemorrhage and exudate detection in automated grading of diabetic retinopathy. Br J Ophthalmol 2010; 94:706–11
34. Karami M, Janghorbani M, Dehghani A, Khaksar K, Kaviani A: Orbital Doppler evaluation of blood flow velocities in patients with diabetic retinopathy. Rev Diabet Stud 2012; 9: 104–11

35. Nandyala SV, Marquez-Lara A, Fineberg SJ, Singh R, Singh K: Incidence and risk factors for perioperative visual loss after spinal fusion. Spine J 2014; 14:1866–72
36. Biousse V, Newman NJ: Ischemic optic neuropathies. N Engl J Med 2015; 372:2428–36
37. Danesh-Meyer HV, Levin LA: Glaucoma as a neurodegenerative disease. J Neuroophthalmol 2015; 35(Suppl 1):S22–8
38. Engler-Chiurazzi EB, Singh M, Simpkins JW: From the 90's to now: A brief historical perspective on more than two decades of estrogen neuroprotection. Brain Res 2016; 1633:96–100
39. Levin LA, Danesh-Meyer HV: Hypothesis: A venous etiology for nonarteritic anterior ischemic optic neuropathy. Arch Ophthalmol 2008; 126:1582–5
40. Houchens R RD, Elixhauser A, Jiang J: Nationwide Inpatient Sample (NIS) Redesign Final Report, HCUP Method Series Report. Available at: http://www.hcup-us.ahrq.gov/reports/methods/methods.jsp. Agency for Healthcare Research and Quality, 2014. Accessed October 5, 2016

ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

Laughing Gas as an American Fundraiser for "Unemployed Veterans" of World War I



Signing his work as "Bill Kenny," an artist contributed this two-panel cartoon to the back cover of *Laughing Gas*, an American fundraising pamphlet "Distributed by Unemployed Veterans." The left panel is captioned "1918—On the Rhine," and features an American "doughboy" standing guard on the bank of the Rhine River. Following World War I, rampant unemployment among American military veterans spurred Congress to pass the World War Adjusted Compensation Act of 1924. Because the act delayed compensation 11 years, many veterans ended up like our now ex-soldier in the right panel, staring at a sign reading "Help / Wanted / Male." Captioned "1925—On the Line," the right panel depicts an unemployed veteran, perhaps one of scores distributing this cartoon's fundraising pamphlet. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

George S. Bause, M.D., M.P.H., Honorary Curator and Laureate of the History of Anesthesia, Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, and Clinical Associate Professor, Case Western Reserve University, Cleveland, Ohio. UJYC@aol.com.