Incidence of and Risk Factors for Perioperative Optic Neuropathy After Cardiac Surgery

Sachin D. Kalyani, MD, Neil R. Miller, MD, Li Ming Dong, PhD,
William A. Baumgartner, MD, Diane E. Alejo, BA, and Timothy B. Gilbert, MD, MBA

Neuro-Ophthalmology Unit, Division of Clinical Trials and Biometry, The Wilmer Eye Institute, Baltimore, Maryland, Division of Cardiac Surgery, The Johns Hopkins Medical Institutions, Baltimore, Maryland, and Departments of Anesthesiology and Medicine (Cardiology), University of Maryland, Baltimore, Maryland

Background. **Visual loss from optic neuropathy rarely occurs in the perioperative period in patients who have undergone nonocular surgery. We performed a retrospective, matched, case–control study to determine the incidence of perioperative optic neuropathy (PON) after cardiac surgery with the use of cardiopulmonary bypass (CPB) and to determine risk factors that may lead to this potentially devastating complication.**

Methods. **Medical records of all patients undergoing cardiac surgery during a 9-year period were reviewed retrospectively to identify visual loss from acute unilateral and bilateral optic neuropathy during the perioperative period that had developed in patients. Data were collected from these patients and compared with data from control subjects matched for age, gender, risk factors for vascular disease, and type of surgery to determine the incidence of and potential risk factors for PON.**

Results. **Of 9701 surgical patients requiring CPB, 11 patients (0.113%) with PON were identified. Although both the absolute and relative drop in hemoglobin during the perioperative period approached statistical significance, no other putative risk factors were identified.**

Conclusions. **The risk of PON associated with cardiac surgery in which CPB is used is low but substantial. The factors that lead to the condition remain unknown, although the presence of systemic vascular disease and both the absolute and relative drop in hemoglobin during the perioperative period seem to be important. Because PON often causes profound permanent visual loss, we recommend that patients, particularly those with systemic vascular disease, for whom cardiac surgery with CPB is planned, be made aware of this potential complication.**

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Visual loss from optic neuropathy occurs in the perioperative period in some patients who have undergone nonocular surgery. Certain types of surgery, particularly cardiac [1] and spinal procedures with the patient in the prone position [2, 3], seem to be associated with an increased risk for this form of visual loss which is believed to be ischemic in origin. Nuttall and associates reported the incidence of perioperative optic neuropathy (PON) in patients undergoing cardiopulmonary bypass (CPB) surgery to be 0.06% and identified several specific risk factors that seemed to be associated with the development of this condition [4]. We performed a retrospective, matched, case–control study to determine the incidence of PON after cardiac surgical procedures requiring CPB and to determine the risk factors that may lead to this potentially devastating complication.

Material and Methods

The Cardiac Surgery Database and the Electronic Patient Record (EPR) of the Johns Hopkins Hospital were used to identify all patients diagnosed with any type of visual loss associated with cardiac surgery with and without cardiopulmonary bypass (CPB) during a 9-year period between July 1, 1993 and June 30, 2002. The medical records of all patients selected in this initial screening process were reviewed to identify visual loss caused by an acute unilateral or bilateral optic neuropathy in the perioperative period. Perioperative optic neuropathy was confirmed by the presence of several findings. For unilateral optic neuropathy, patients demonstrated a unilateral decrease in visual acuity, dyschromatopsia, a visual field defect, and a relative afferent pupillary defect (RAPD). Such patients had either a normal-appearing optic disc (retrobulbar optic neuropathy) or a swollen optic disc (anterior optic neuropathy) in the affected eye. For bilateral optic neuropathy, patients demonstrated the presence of bilateral and newly reduced visual acuity, bilateral dyschromatopsia, bilateral visual field defects, and a RAPD or pupils that were sluggishly reactive or nonreactive to light stimulation. Such patients also had swollen optic discs, normal-appearing optic discs that subsequently became pale, or one swollen optic disc and one normal-appearing optic disc that subsequently became pale.

For each patient case of perioperative optic neuropathy (PON), 2 or 3 control subjects were selected at random

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Address reprint requests to Dr Miller, Maumenee B-109, Wilmer Eye Institute, Johns Hopkins Hospital, 600 N Wolfe St, Baltimore, MD 21287; e-mail: nrmiller@jhmi.edu.

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Table 1. Distribution of Categorical Variables by Case and Control

Variable	Patient Case (%) N = 11	Control Subject (%) N = 30
Male gender	9 (82)	25 (83)
Diabetes	5 (45)	12 (40)
Hypertension	10 (91)	27 (90)
Hyperlipidemia	6 (55)	19 (63)
Smoker[a]	6 (55)	24 (80)
Vascular disease[a]	5 (45)	9 (30)

[a] Not used in matching; all others were used for matching case and control.

from among patients who underwent cardiac surgery but who did not experience perioperative visual loss. Control subjects were matched for the following factors: (i) age, (ii) gender, (iii) type of surgery, (iv) presence or absence of diagnosed hypertension, (v) presence or absence of diagnosed diabetes mellitus, and (vi) presence or absence of diagnosed hyperlipidemia. A history of clinically severe vascular disease was defined as claudication, thoracic aneurysm, abdominal aortic aneurysm, history of previous peripheral vascular surgery, transient ischemic attack, cerebral vascular accident, carotid artery stenosis, or previous carotid endarterectomy as suggested by Nuttall and associates [4].

Medical records of both the patient case and control subjects were reviewed and potential risk factors for blindness were abstracted. The overall frequency of PON was calculated by dividing the number of observed patient cases of PON by the total number of procedures during the study period. For the case–control analysis, potential risk factors for visual loss were assessed using conditional logistic regression. Collected data were tabulated and normalized in Splus 5 (MathSoft, Seattle, WA). Statistical calculations and tests of significance were performed using SAS V8 (SAS Institute, Inc., Cary, NC). *P* values of less than 0.05 were considered significant.

Results

The distribution of categorical variables according to patient case versus control subject is shown in Table 1. Eleven patient cases of PON were identified among 9701 cardiac surgical procedures requiring CPB performed during the 9-year study period for an incidence of 0.113%. No patient cases of PON occurred among 205 cardiac surgical procedures in which CPB was not used.

The 11 patients who experienced PON included 9 men and 2 women. The mean age at time of surgery was 58.8 years (range, 39–81 years). Results of their perioperative ophthalmological examinations are detailed in Table 2. Visual loss was unilateral in 8 patients and bilateral in 3 patients. Optic disc swelling was noted in 7 of 8 patients with unilateral vision loss and in 1 of 3 patients with bilateral vision loss. No patient with evidence of a bilateral optic neuropathy had optic disc swelling in one eye and a normal-appearing optic disc in the other. Thus, 7 of 8 patients with unilateral PON had an anterior process, whereas 1 patient had a posterior (retrobulbar) PON. Of the 3 patients with bilateral PON, 1 had bilateral anterior PON and the remaining 2 had bilateral posterior PON.

Table 3 presents the summary statistics for risk factors and the results of conditional logistic regression analysis for our matched case–control series. The relative risks (RR) for each measured variable are listed in the far right column of the table. No potential risk factors yielded statistical significance (ie, $p < 0.05$); however, patients with vascular disease had more than twice the risk of PON compared with patients without vascular disease (RR = 2.22, $p = 0.32$). Furthermore, the absolute drop in hemoglobin (Hgb)—defined as the preoperative Hgb minus the lowest postoperative Hgb—approached statistical significance (RR = 1.45, $p = 0.06$).

Comment

Perioperative optic neuropathy is a potentially devastating complication of any surgical procedure, in part because it often produces severe visual loss and in part because once vision is lost, it rarely recovers. In addition, there is no known treatment for PON. We found the incidence of PON associated with cardiac surgery using CPB at the Johns Hopkins Hospital to be 0.113%. Although this may seem low, it is substantially higher than the reported incidence of PON (0.0008%) associated with noncardiac procedures found by Warner and associates [5]. In addition, it is almost twice that reported by Nuttall and associates who found a PON incidence of 0.06% in patients undergoing cardiac surgical procedures requiring CPB [4] at the Mayo Clinic. Nuttall and associates also found evidence of an increase in the frequency of PON over their study period between 1976 and 1994. Our study considered patients who underwent surgery from 1993–2002. As the study period in our series was more recent than that of Nuttall and associates [4], our findings of an increased incidence of PON associated with cardiac sur-

Table 2. Results of Postoperative Eye Examination

	Affected Eye			Optic Disc Swelling Present Vs Absent (Eye Affected)
	OD	OS	OU	
1		X		Present (OS)
2			X	Present (OU)
3		X		Present (OS)
4	X			Present (OD)
5			X	Absent
6		X		Present (OS)
7		X		Present (OS)
8		X		Present (OS)
9		X		Absent
10			X	Absent
11		X		Present (OS)

OD = right eye; OS = left eye; OU = both eyes.

Table 3. Summary of Risk Factors and Its Estimated Effect for PON Using Conditional Logistic Regression for Matched Case–Control

Variables	Mean (SD)	Estimate of Coefficient	Standard Error	P value	Relative Risk
Smoker	. . .	−1.70	1.15	0.14	0.18
Vascular disease	. . .	0.80	0.80	0.32	2.22
(Preop Hgb–lowest intraop Hgb)/(preop Hgb)[a]					
Case	38 (88)				
Control	33 (13)	0.05	0.04	0.22	1.05
Preop Hgb–lowest intraop Hgb					
Case	5.1 (1.7)	0.32	0.24	0.18	1.38
Control	4.3 (1.9)				
Preop Hgb–Hgb immediately postop)/(preop Hgb)[a]					
Case	23 (14)	0.02	0.02	0.30	1.03
Control	17 (18)				
Preop Hgb–Hgb immediately postop					
Case	3.3 (2.3)	0.20	0.17	0.24	1.22
Control	2.4 (2.3)				
(Preop Hgb–lowest postop Hgb)/(preop Hgb)[a]					
Case	32 (15)	0.06	0.03	0.07	1.06
Control	21 (16)				
Preop Hgb–lowest postop Hgb					
Case	4.5 (2.6)	0.37	0.20	0.06	1.45
Control	2.9 (2.1)				
Fluid in–fluid out (in ml)					
Case	1569 (1663)	0.00	0.00	0.14	1.00
Control	2331 (1434)				

[a] Expressed as percent.

Hgb = Hemoglobin; PON = perioperative optic neuropathy; SD = standard deviation.

gery with CPB are consistent with their belief that the frequency of PON is continuing to rise.

In this study, we compared patients with PON with control subjects matched for age, gender, and systemic vascular diseases including diabetes mellitus, hypertension, and hyperlipidemia, as well as the specific type of cardiac surgery in an effort to identify potential risk factors for PON. Although no *p* values reached statistical significance, there were some important trends. Similar to the study by Nuttall and associates [4], patients with vascular disease in our study were more likely to have PON, typically a more than doubled relative risk compared with patients without vascular disease. In addition, the difference between preoperative hemoglobin and lowest postoperative hemoglobin was found to have a RR of 1.149 and was close to statistical significance ($p = 0.063$). This suggests that a larger perioperative drop in hemoglobin might be associated with an increased risk of PON. The fact that there were only 11 patient cases of PON may explain why no *p* value reached statistical significance. Continuous collection of data in the future will provide more evidence about our findings.

No patient cases of PON occurred at our institution after cardiac surgery without CPB. Although this may simply reflect the small number of patient cases performed without CPB, there are several reasons why CPB itself might be a risk factor for PON. First, CPB requires cannulation and cross clamping of the aorta—either of which can result in thromboembolism to the retinal arteries or central visual centers [6]. Blauth and associates demonstrated this CPB-based phenomenon graphically using fluorescein retinography. They illustrated that enhanced showering of thromboemboli occurs during initiation of CPB and also is related to the method of carbon dioxide management (eg, α-stat vs pH-stat) [6] and type of oxygenator used in the procedure [7]. Indeed, one of the potential benefits of "off-pump" procedures is the reduction or elimination of such thromboemboli by reducing manipulation of the aorta which is frequently diseased in patients undergoing revascularization procedures.

Patient cases requiring CPB are also associated with lower postoperative hemoglobin levels than "off-pump" patient cases because of hemodilution by the pump prime and possibly because of greater blood loss [8]. This could result in reduced retinal or cerebral levels of oxygen supply and potentially lead to ischemia. Other potential risk factors for PON during cardiac surgery with CPB include hypotension, arrhythmias, hypocoagulability, and tissue edema which are generally more common when CPB is used.

Mild-to-moderate hypothermia is commonly used in patient cases requiring CPB and the resultant decrease in blood flow may predispose the optic nerves to ischemia. Indeed, cerebral blood flow decreases 6%–7% with each centigrade degree drop in temperature [9]. CPB causes disturbances of coagulation and hemostasis. Extracorporeal circulation of blood within bioprosthetic membranes during CPB promotes the activation of the complement system leading to increased concentrations of C_3A—a smooth-muscle spasmogen [10]. In fact, serum concentrations of this vasoconstrictor are more than five times higher after termination of CPB and may contribute to the "postpump syndrome" [10].

In conclusion, the incidence of PON after cardiac procedures in which CPB is employed is rare but considerable. We therefore believe that consideration should be given to making patients aware of this potentially devastating complication—particularly if they have clinically severe vascular disease. In addition, it seems prudent to avoid large decreases in perioperative hemoglobin levels.

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