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Perioperative Retinal Artery Occlusion:

Risk Factors in Cardiac Surgery from the United States National Inpatient Sample 1998– 2013

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Abstract

Purpose—To study the incidence and risk factors for retinal artery occlusion (RAO) in cardiac surgery.

Design—Retrospective study using the National Inpatient Sample (NIS).

Author Contributions:

Data collection: Calway, Rubin, Roth

Analysis and interpretation: Calway, Rubin, Moss, Joslin, Beckmann, Roth

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Conception and design: Calway, Rubin, Moss, Roth

Overall responsibility: Calway, Rubin, Moss, Joslin, Beckmann, Roth

Methods—The NIS was searched for cardiac surgery. Retinal artery occlusion was identified by International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. Postulated risk factors based on literature review were included in multivariate logistic models.

Main Outcome Measures—Diagnosis of RAO.

Results—A total of 5 872 833 cardiac operative procedures were estimated in the United States from 1998 to 2013, with 4564 RAO cases (95% confidence interval [95% CI], 4282–4869). Nationally estimated RAO incidence was 7.77/10 000 cardiac operative procedures from 1998 to 2013 (95% CI, 7.29–8.29). Associated with increased RAO were giant cell arteritis (odds ratio [OR], 7.73; CI, 2.78–21.52; P < 0.001), transient cerebral ischemia (OR, 7.67; CI, 5.31–11.07; P < 0.001), carotid artery stenosis (OR, 7.52; CI, 6.22–9.09; P < 0.001), embolic stroke (OR, 4.43; CI, 3.05–6.42; P < 0.001), hypercoagulability (OR, 2.90; CI, 1.56–5.39; P < 0.001), myxoma (OR, 2.43; CI, 1.39–4.26; P = 0.002), diabetes mellitus (DM) with ophthalmic complications (OR, 1.89; CI, 1.10–3.24; P = 0.02), and aortic insufficiency (OR, 1.85; CI, 1.26–2.71; P = 0.002). Perioperative bleeding, aortic and mitral valve surgery, and septal surgery increased the odds of RAO. Negatively associated with RAO were female gender (OR, 0.77; CI, 0.66–0.89; P < 0.001), thrombocytopenia (OR, 0.79; CI, 0.62–1.00; P = 0.049), acute coronary syndrome (OR, 0.72; CI, 0.58–0.89; P = 0.003), atrial fibrillation (OR, 0.82; CI, 0.70–0.95; P = 0.01), congestive heart failure (OR, 0.73; CI, 0.60–0.88; P < 0.001), DM 2 (OR, 0.74; CI, 0.61–0.89; P = 0.001), and smoking (OR, 0.82; CI, 0.70–0.97; P = 0.02).

Conclusions—Risk factors for RAO in cardiac surgery include giant cell arteritis, carotid stenosis, stroke, hypercoagulable state, and DM with ophthalmic complications; associated with lower risk were female gender, thrombocytopenia, acute coronary syndrome, atrial fibrillation, congestive heart failure, DM 2, and smoking. Surgery in which the heart was opened (e.g., septal repair) versus surgery in which it was not (e.g., CABG) and perioperative bleeding increased the risk of RAO.

Perioperative visual loss is a rare but devastating complication that occurs more frequently in spine and cardiac surgery versus other surgical procedures.¹ Although ischemic optic neuropathy is the most common type of perioperative visual loss after spinal surgery,² retinal artery occlusion (RAO) is thought to occur more frequently after cardiac surgery, possibly because of emboli.³ The existence of retinal microembolization in cardiac surgery is well known⁴; however, long-term outcomes of this phenomena and risk factors for RAO in cardiac surgery have not been quantitated. We recently estimated that RAO after spine fusion surgery occurs at a rate of 0.89/10 000 in the United States,⁵ but it may be higher after cardiac surgery according to sparse previous estimates.^{6,7} The impact of perioperative RAO on a patient's life is considerable, because the usual outcome includes visual loss and is generally not reversible.⁸ With cardiac surgery, one of the most commonly performed inhospital surgical procedures in the United States,¹ identification of risk factors for perioperative RAO is imperative.

Perioperative RAO is difficult to treat successfully, and understanding its mechanisms may aid in identifying high-risk patients.⁹ In turn, this could prompt modification of the informed consent and the surgical planning. Furthermore, perioperative RAO could serve as a model

for the study of the natural history of retinal vascular disease because it occurs in the more closely monitored hospital environment.

Spontaneous nonperioperative RAO is associated with stroke, coronary artery disease, atrial fibrillation, and carotid stenosis, conditions frequently present in patients who require heart surgery, particularly coronary artery bypass grafting (CABG).^{3,10,11} Associations also have been documented for spontaneously developing RAO and hypercoagulable state, ¹² valvular heart disease,¹³ and myxoma.^{14,15} Accordingly, we hypothesized that risk factors for RAO after cardiac surgery resemble those of spontaneous RAO.¹⁶ Moreover, a higher risk of RAO would be anticipated in procedures in which emboli are likely to develop, that is, with air emboli when the heart is opened for valve or septal surgery.¹⁷ Embolism also can be due to dislodging of atherosclerotic plaque from the aorta during arterial cannulation for cardiopulmonary bypass or in aortic valve surgery.¹⁸ Another potential cause of perioperative RAO is thrombosis within the arterial circulation due to, for example, a hypercoagulable state, decreased perfusion in the microcirculation, or damaged vascular endothelium, conditions that may occur with cardiac surgery.^{19,20} By examining the National Inpatient Sample (NIS), we studied potential risk factors for perioperative RAO in cardiac surgery. Our aims were to determine the trends in incidence and identify the associated patient characteristics, surgical, and perioperative factors.

Methods

The NIS is an approximately 20% stratified sample of nonfederal inpatient hospital discharge data, maintained by the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality. Patient information includes demographics, diagnoses (principal and secondary), procedures (principal and secondary), charges (US dollars), length of stay (in days), discharge status, outcomes, and medical diagnoses. There are no specific patient identifiers. Therefore, the Institutional Review Boards of the University of Chicago and the University of Illinois deemed this study "exempt."

Discharge data in the NIS from 1998 to 2013 were studied. Starting in 2012, to improve accuracy of national estimates, all hospitals were included. Thus, we used Agency for Healthcare Research and Quality 1998–2013 "trend weights" (hcupnet.ahrq.gov) to ensure accurate weighting,²¹ as previously described.⁵ The "Survey" function (StataCorp LP, College Station, TX) was used for patient-level analyses. Diagnoses and procedures are coded using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; http://www.cdc.gov/nchs/icd/icd9cm.htm).

Data Classification

Discharges including ICD-9-CM codes for CABG, valve replacement or repairs adjacent to valves, left ventricular assist device, heart transplant, ventricular or atrial septal repairs, cardiopulmonary bypass, and pericardiectomy were evaluated (Table S1, available at www.aaojournal.org). Among these, CABG and pericardiectomy do not necessitate opening of the heart. To ensure complete coverage, ICD-9-CM codes were confirmed against Current Procedural Technology (Table S1, available at www.aaojournal.org) cardiac surgery codes using EncoderPro.com (Optum, Salt Lake City, UT). Patients discharged with a primary or

secondary diagnostic ICD-9-CM code for RAO (362.30–34) and a relevant cardiac surgical procedure code were considered to have developed RAO during the hospitalization.

Missing Data

To account for missing data in the multivariate analysis, multiple (10) imputations by chained equations were performed using Stata.²² Gender, age, race, and type of admission were included in the imputation model. Discharge status was not included in the regression analysis, because it was deemed improbable to affect development of RAO.

Patient Characteristics

Patient characteristics analyzed included age (years, continuous variable), gender, length of hospital stay (days), yearly inflation-adjusted total hospital charges (both as continuous variables), type of admission (elective vs. nonelective), discharge status (routine, short-term hospital, home healthcare, died, other), and race. For age, 10-year epochs were used (i.e., 18-30 years, 31-40 years). Previous studies have suggested that cardiopulmonary bypass is a significant factor for RAO; however, there are no comprehensive studies on perioperative RAO in cardiac surgery.²³ Therefore, we identified potential risk factors for RAO on the basis of previous case series, large database reviews, and case reports on spontaneous RAO as recommended in the Strengthening the Reporting of Observational Studies in Epidemiology statement.²⁴ Medical diagnoses (ICD-9-CM codes in Table S2, available at www.aaojournal.org) studied were coronary artery disease,¹¹ carotid artery stenosis,^{10,11} diabetes mellitus (DM) type 1 and 2 without complications,³ DM with complications (ophthalmic, renal, or neurologic),²⁵ hypertension,¹⁰ hypertension with cardiac complications,²⁶ obesity,¹⁰ peripheral vascular disease, smoking,²⁷ myxoma,^{14,15} congestive heart failure, atrial fibrillation,¹¹ giant cell arteritis,²⁸ acute coronary syndrome,²⁹ ventricular septal defect, ³⁰ atrial/mitral stenosis and/or insufficiency, ¹³ cardiomyopathy, thrombocytopenia, and hypercoagulable state (including primary and secondary hypercoagulable states, homocystinuria, and presence of antiphospholipid antibodies).^{12,31,32} Hospital conditions included anemia, transfusion, cardiogenic shock, and postoperative bleeding. Stroke was included as embolic, thrombotic, transient ischemia, and "other."33

Analysis

Patient characteristics, surgical factors, and RAO from 1998 to 2013 were tabulated using national estimates. Multivariate logistic regression was conducted with RAO as the dependent variable and risk factors and surgery types as independent variables. We included discharges in which a patient underwent 2 or more cardiac operative procedures during the hospitalization (e.g., CABG and valve). Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs). A second multivariate model was conducted in the same manner, but eliminated from analysis were discharges in which 2 cardiac operative procedures were performed on the same subject (i.e., an alternate "single procedure" model).

The proportions of patients affected by RAO as a function of the surgical procedure (CABG vs. valve vs. septal surgery) were compared using the chi-square test. To further examine the influence of opening of the heart as a risk for RAO, incidence was compared using chi-

square, among patients undergoing CABG alone with those undergoing patent foramen ovale closure and CABG (ICD-9-CM: 35.71). Because CABG was a common feature, it could be assumed that the comparison at least partially adjusted for severity of underlying illness.

A *P* value < 0.05 was considered significant. The variance inflation factor examined for collinearity; variance inflation factor < 10 indicates lack of collinearity.⁵ Stata v14.0-MP (StataCorp LP) was used for all statistical analyses except power analysis, for which we used G-Power (http://gpower.hhu.de/).

Results

An estimated 5 872 833 operative cardiac procedures were performed in the United States from 1998 to 2013, of which 4564 patients (CI, 4282–4869) had a diagnosis of RAO. The overall RAO incidence was 7.77 cases per 10 000 procedures (CI, 7.29–8.29). Incidence (Table 1) ranged from a low of 5.11/10 000 (CI, 3.87–6.90) in 2001 to 11.00 (CI, 8.70–14.14) in 2012, with no significant change over time (P= 0.81).

Table 2 shows the cardiac procedures and incidence of RAO from 1998 to 2013. Retinal artery occlusion was most common among operations on the atrial and ventricular septae (22.65/10 000; CI, 18.12–28.70), less common with CABG (6.02/10 000; CI, 5.55–6.55), and least common with heart transplantation (3.65/10 000; CI, 0.79–36.72). There was a significant difference (P < 0.001) in the proportion of patients with RAO in valve surgery versus CABG and in CABG compared with septal surgery. When comparing CABG alone versus CABG with patent foramen ovale closure, the incidence of RAO was 5.52/10 000 (CI, 5.03–6.06) compared with 15.10/ 10 000 (CI, 4.72–74.56), respectively. However, although a trend, the difference was not significant (P = 0.084).

With the sample size and the incidence of RAO both known, a post hoc logistic regression power analysis was performed to estimate detection limits of the OR calculations. Because RAO was rare (7.8/10 000), analysis was adjusted with Hseih and colleagues' formula.³⁴ For detecting the influence of potential risk factors with low prevalence (1%), such as vision-threating diabetic retinopathy,³⁵ the database was adequately powered ($\alpha = 0.05$, power = 80%) to detect an OR as low as 1.3. With more prevalent risk factors (40%) such as hypertension,³⁶ an OR as low as 1.1 could be robustly detected ($\alpha = 0.05$, power = 80%).

Table 3 details the characteristics of patients who underwent cardiac surgery, and the multivariate model results are shown in Table 4 (nonsignificant covariates appear in Table S3, available at www.aaojournal.org). Conditions most strongly associated with increased RAO after cardiac surgery were giant cell arteritis (OR, 7.73; CI, 2.78–21.52; P < 0.001), transient cerebral ischemia (OR, 7.67; CI, 5.31–11.07; P < 0.001), carotid artery stenosis (OR, 7.52; CI, 6.22–9.09; P < 0.001), embolic stroke (OR, 4.43; CI, 3.05–6.42; P < 0.001), hypercoagulable state (OR, 2.90; CI, 1.56–5.39; P < 0.001), myxoma (OR, 2.43; CI, 1.39–4.26; P = 0.002), DM with ophthalmic complications (OR, 1.89; CI, 1.10–3.24; P = 0.02), and aortic insufficiency (OR, 1.85; CI, 1.26–2.71; P = 0.002).

The following were negatively associated with RAO: thrombocytopenia (OR, 0.79; CI, 0.62–1.00; P = 0.049), female gender (OR, 0.77; CI, 0.66–0.89; P < 0.001), acute coronary syndrome (OR, 0.72; CI, 0.58–0.89; P = 0.003), atrial fibrillation (OR, 0.82; CI, 0.70–0.95; P = 0.01), congestive heart failure (OR, 0.73; CI, 0.60–0.88; P < 0.001), DM 2 (OR, 0.74; CI, 0.61–0.89; P = 0.001), and smoking (OR, 0.82; CI, 0.70–0.97; P = 0.02).

Postoperative bleeding was associated with RAO (OR, 1.34; CI, 1.13–1.58; P= 0.001). Specific surgical procedures associated with RAO included aortic valve (OR, 1.58; CI, 1.29–1.95; P< 0.001), mitral valve (OR, 1.68; CI, 1.34–2.10; P< 0.001), and septal surgery (OR, 2.16; CI, 1.62–2.87; P< 0.001), all of which involve surgical opening of the heart. Coronary artery bypass grafting was negatively associated with RAO (OR, 0.61; CI, 0.48–0.79; P< 0.001). Use of cardiopulmonary bypass did not influence RAO. The single and multiple procedure models yielded nearly identical results, except that in the single-procedure model, ORs for 1 parameter were nonsignificant (aortic valve surgery, OR, 1.03; CI, 0.79–1.34; P= 0.82).

Discussion

We found that RAO incidence was 7.77 per 10 000 cardiac surgery procedures from 1998 to 2013. That RAO accompanies these procedures has been known for decades,²³ but the present study is the first to determine its incidence and risk factors, and is also the largest study to date of perioperative RAO. By comparison, the rate of RAO we found in cardiac surgery is approximately 10 times that in spinal fusion, another surgical procedure in which visual loss is more common.⁵ Diabetes mellitus with ophthalmic complications (primarily diabetic retinopathy), carotid stenosis, embolic stroke, transient cerebral ischemia, giant cell arteritis, myxoma, aortic insufficiency, and hypercoagulable state was the patient factor that conferred a higher odds of developing RAO. Postoperative bleeding and specific surgical types, including valve surgery and surgery on the atrial or ventricular septa, were associated with a higher risk of RAO. Age had no impact, and female gender was associated with lower risk.

Cardiovascular risk factors, including carotid stenosis and stroke, have long been associated with spontaneous RAO,¹⁰ but documentation of any association with perioperative RAO is lacking. Risk factors for stroke in cardiac surgery have been well described, including cerebrovascular disease, peripheral arterial disease, DM, hypertension, prior cardiac surgery, preoperative infection, urgent operation, cardiopulmonary bypass time >2 hours, intraoperative hemofiltration, and high transfusion requirement.^{16,37,38} Many of these factors did not confer a heightened risk of RAO in the present study, rather atherosclerotic factors for RAO were limited to carotid stenosis, embolic stroke, transient cerebral ischemia, and aortic insufficiency. Surprisingly, cardiopulmonary bypass had no influence on RAO.

Systemic hemodynamic factors also may contribute, particularly when perioperative hypotension is present with significant carotid stenosis.³ Supporting this notion in our study was increased RAO in those who sustained postoperative bleeding, often a surrogate for events such as anemia and decreased O_2 delivery, with attendant damage to the

microvasculature. Thrombocytopenia, which could increase bleeding, but also conversely decrease emboli, was associated with a lower risk of RAO.

The increased incidence and OR for RAO when the heart is opened, including valvular heart surgery, myxoma, foramen ovale repair, or septal wall surgery, suggest a prominent role for embolism.¹⁷ Coronary artery bypass grafting resulted in fewer strokes than surgery on the aortic or mitral valves,¹⁶ an outcome aligning with our findings. Also in agreement with our results, atheromatous plaque is another principal cause of embolism and poorer outcomes during surgery on the aortic valve.^{39,40} However, our analysis comparing CABG with and without foramen ovale repair, the main difference being opening of the heart, found that there was a trend but not a significant difference in RAO incidence.

Because opening the heart is an important influence on the risk of stroke and RAO,^{41–43} transcranial Doppler might be effective in characterizing emboli and providing guidance for intraoperative intervention.⁴⁴ However, its use has not altered the outcomes for cerebral complications, specifically, cognitive deficit.⁴⁵ Because the ophthalmic artery is the first intracranial branch of the internal carotid artery, it is rational to expect stroke and RAO-induced vision loss to coexist in high-risk subjects. However, the data in the present study do not allow this hypothesis to be tested.

It seems logical that a hypercoagulable state also would increase the risk of RAO by facilitating arterial thrombus formation. Although our results agree with previous smaller studies showing increased spontaneous RAO,^{12,31,32} ICD-9-CM codes do not allow sufficient resolution to identify a specific defect (e.g., Factor V Leiden mutation) that is responsible. In contrast, a common source of emboli, atrial fibrillation, resulted in a lower risk. It is not possible to differentiate between preoperative and postoperative atrial fibrillation, the latter of which occurs in 15% to 50% of cardiac surgical procedures.⁴⁶ Therefore, caution should be exercised when interpreting this finding.

Vasculitis also is associated with RAO,^{29,33} including giant cell arteritis, which had the highest OR among all RAO risk factors in the present study. Giant cell arteritis has been implicated in ocular syndromes, including blindness,²⁸ and is often accompanied by other vascular diseases; thus, it may be a marker for vascular disease. It is unclear whether patients were diagnosed with giant cell arteritis before developing RAO or the RAO diagnosis led clinicians to diagnose giant cell arteritis as well.

Although DM has been cited as a risk factor for RAO,³ surprisingly, uncomplicated DM 2 was associated with a decreased risk of RAO. However, the result should be interpreted cautiously, because in one study in adolescents, coding for DM 2 had a low positive predictive value.⁴⁷ Female gender has been shown to result in a lower incidence of spontaneous RAO and was also the case in our study.^{13,48} The reason for the "protective" effect of female gender is not clear and may be due to an influence of estrogen or other as yet unknown factors.

Both congestive heart failure and acute coronary syndrome were associated with lower risk for RAO. Acute coronary syndrome has been linked with RAO,⁴⁹ and the risk of atherosclerosis and RAO is well established. However, the ICD-9-CM codes included

subsequent visits for myocardial infarctions. It is possible that patients receiving treatment for past coronary events are at a lowered risk because of treatment, but it is impossible to ascertain how close to the time of surgery that events occurred.

Before definitively concluding that patient conditions common to RAO in cardiac surgery confer a higher risk, including DM with ophthalmic complications, carotid stenosis, and stroke, there are caveats. It is likely that many, if not all, patients who developed RAO subsequently underwent a detailed neurologic and ophthalmologic examination, although this is indeterminate in the NIS. Diabetic retinopathy would be readily detectable by a trained examiner. Likewise, visual loss, particularly if unilateral, likely would prompt testing for carotid stenosis. Thus, the association of diabetic eye complications and carotid stenosis with RAO might partly reflect a heightened diagnosis intensity.

Study Limitations

The NIS is an administrative database of discharge records and is susceptible to undocumented diagnoses, overdiagnosis or underdiagnosis, and coding errors. The severity of visual loss and unilateral or bilateral involvement cannot be determined. Longitudinal follow-up for progression or improvement is not possible. Because this was an observational study, it is limited to identifying risk factors associated with an increased OR of RAO after surgery and cannot conclusively determine the cause and effect. The study cannot definitively distinguish between prehospital admission RAO and RAO that developed during the hospitalization. However, the incidence of RAO in the population (~1/100 000) is far less than the results in the present study,⁸ suggesting that our findings reflect a new diagnosis. Our study has considerable predictive power, given a population of approximately 6 million and approximately 5000 estimated RAO cases.

In conclusion, specific patient factors, including DM with ophthalmic complications (in particular diabetic retinopathy), giant cell arteritis, stroke, carotid stenosis, and hypercoagulability, are associated with RAO in patients undergoing cardiac surgery. Screening for retinal vascular disease and carotid artery stenosis may aid in identifying the high-risk patient, providing proper surgical informed consent, and potentially altering the surgical plan. Longitudinal studies are required to identify relative and additive effects of risk factors, and longer-term outcomes after perioperative RAO. Studies in the perioperative environment could afford a unique window into the natural history of RAO and provide greater insight into potential treatment options.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Abbreviations and Acronyms

CABG	coronary artery bypass grafting
CI	confidence interval
DM	diabetes mellitus

ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical
	Modification

- NIS National Inpatient Sample
- **OR** odds ratio
- **RAO** retinal artery occlusion

References

- 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; 109:1534–1545. [PubMed: 19713263]
- Lee MJ, Konodi MA, Cizik AM, et al. Risk factors for medical complication after spine surgery: a multivariate analysis of 1,591 patients. Spine J. 2012; 12:197–206. [PubMed: 22245448]
- Hayreh SS, Podhajsky PA, Zimmerman MB. Retinal artery occlusion: associated systemic and ophthalmic abnormalities. Ophthalmology. 2009; 116:1928–1936. [PubMed: 19577305]
- 4. Blauth C, Arnold J, Kohner EM, Taylor KM. Retinal microembolism during cardiopulmonary bypass demonstrated by fluorescein angiography. Lancet. 1986; 2:837–839. [PubMed: 2876281]
- Rubin DS, Parakati I, Lee LA, et al. 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; 125:457–464. [PubMed: 27362870]
- 6. Shaw PJ, Bates D, Cartlidge NE, et al. Neuro-ophthalmological complications of coronary artery bypass graft surgery. Acta Neurol Scand. 1987; 76:1–7. [PubMed: 3498286]
- Ascione R, Ghosh A, Reeves BC, et al. Retinal and cerebral microembolization during coronary artery bypass surgery: a randomized, controlled trial. Circulation. 2005; 112:3833–3838. [PubMed: 16365207]
- 8. Varma DD, Cugati S, Lee AW, Chen CS. A review of central retinal artery occlusion: clinical presentation and management. Eye (Lond). 2013; 27:688–697. [PubMed: 23470793]
- 9. Schrag M, Youn T, Schindler J, et al. Intravenous fibrinolytic therapy in central retinal artery occlusion: a patient-level meta-analysis. JAMA Neurol. 2015; 72:1148–1154. [PubMed: 26258861]
- Callizo J, Feltgen N, Pantenburg S, et al. Cardiovascular risk factors in central retinal artery occlusion: results of a prospective and standardized medical examination. Ophthalmology. 2015; 122:1881–1888. [PubMed: 26231133]
- Yen JC, Lin HL, Hsu CA, et al. Atrial fibrillation and coronary artery disease as risk factors of retinal artery occlusion: a nationwide population-based study. Biomed Res Int. 2015; 2015:374616. [PubMed: 26558268]
- Chapin J, Carlson K, Christos PJ, DeSancho MT. Risk factors and treatment strategies in patients with retinal vascular occlusions. Clin Appl Thromb Hemost. 2015; 21:672–677. [PubMed: 24335246]
- Schmidt D, Hetzel A, Geibel-Zehender A, Schulte-Monting J. Systemic diseases in noninflammatory branch and central retinal artery occlusion–an overview of 416 patients. Eur J Med Res. 2007; 12:595–603. [PubMed: 18024271]
- 14. Salehian O, Demers C, Patel A. Atrial myxoma presenting as isolated unilateral blindness: a case report and review of the literature. Can J Cardiol. 2001; 17:898–900. [PubMed: 11521132]
- Schmidt D, Hetzel A, Geibel-Zehender A. Retinal arterial occlusion due to embolism of suspected cardiac tumors-report on two patients and review of the topic. Eur J Med Res. 2005; 10:296–304. [PubMed: 16055401]
- Bucerius J, Gummert JF, Borger MA, et al. Stroke after cardiac surgery: a risk factor analysis of 16,184 consecutive adult patients. Ann Thorac Surg. 2003; 75:472–478. [PubMed: 12607656]
- 17. Barbut D, Hinton RB, Szatrowski TP, et al. Cerebral emboli detected during bypass surgery are associated with clamp removal. Stroke. 1994; 25:2398–2402. [PubMed: 7974579]

- Lee R, Matsutani N, Polimenakos AC, et al. Preoperative noncontrast chest computed tomography identifies potential aortic emboli. Ann Thorac Surg. 2007; 84:38–42. [PubMed: 17588379]
- Edelman JJ, Reddel CJ, Kritharides L, et al. Natural history of hypercoagulability in patients undergoing coronary revascularization and effect of preoperative myocardial infarction. J Thorac Cardiovasc Surg. 2014; 148:536–543. [PubMed: 24280714]
- Bicer M, Senturk T, Yanar M, et al. Effects of off-pump versus on-pump coronary artery bypass grafting: apoptosis, inflammation, and oxidative stress. Heart Surg Forum. 2014; 17:E271–E276. [PubMed: 25367242]
- 21. Agency for Healthcare Research and Quality. Overview of the National (Nationwide) Inpatient Sample (NIS). Vol. 2016. Rockville, MD: 2015.
- 22. Houchens, R. HCUP Methods Series Report # 2015-01 ONLINE. U.S. Agency for Healthcare Research and Quality; 2015. Missing Data Methods for the NIS and the SID. https://www.hcupus.ahrq.gov/reports/methods/2015_01.pdf
- Trethowan BA, Gilliland H, Popov AF, et al. A case report and brief review of the literature on bilateral retinal infarction following cardiopulmonary bypass for coronary artery bypass grafting. J Cardiothorac Surg. 2011; 6:1–6. [PubMed: 21208441]
- von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008; 61:344–349. [PubMed: 18313558]
- 25. Chen SN, Chao CC, Hwang JF, Yang CM. Clinical manifestations of central retinal artery occlusion in eyes of proliferative diabetic retinopathy with previous vitrectomy and panretinal photocoagulation. Retina. 2014; 34:1861–1866. [PubMed: 24743637]
- 26. Parsons-Smith G. Sudden blindness in cranial arteritis. Br J Ophthalmol. 1959; 43:204–216. [PubMed: 13638514]
- Cheung N, Lim L, Wang JJ, et al. Prevalence and risk factors of retinal arteriolar emboli: the Singapore Malay Eye Study. Am J Ophthalmol. 2008; 146:620–624. [PubMed: 18639861]
- Hayreh SS, Podhajsky PA, Zimmerman B. Ocular manifestations of giant cell arteritis. Am J Ophthalmol. 1998; 125:509–520. [PubMed: 9559737]
- Chang YS, Chu CC, Weng SF, et al. The risk of acute coronary syndrome after retinal artery occlusion: a population-based cohort study. Br J Ophthalmol. 2015; 99:227–231. [PubMed: 25147366]
- 30. Yuan SM, Shinfeld A, Raanani E. Mitral valve thrombus, embolic events, carotid artery stenosis and patent foramen ovale. Cardiol J. 2008; 15:467–470. [PubMed: 18810724]
- 31. Palmowski-Wolfe AM, Denninger E, Geisel J, et al. Antiphospholipid antibodies in ocular arterial and venous occlusive disease. Ophthalmologica. 2007; 221:41–46. [PubMed: 17183200]
- 32. Chua B, Kifley A, Wong TY, Mitchell P. Homocysteine and retinal emboli: the Blue Mountains Eye Study. Am J Ophthalmol. 2006; 142:322–324. [PubMed: 16876518]
- 33. Rim TH, Han J, Choi YS, et al. Retinal artery occlusion and the risk of stroke development: twelve-year nationwide cohort study. Stroke. 2016; 47:376–382. [PubMed: 26742801]
- Hsieh FY, Bloch DA, Larsen MD. A simple method of sample size calculation for linear and logistic regression. Stat Med. 1998; 17:1623–1634. [PubMed: 9699234]
- Kempen JH, O'Colmain BJ, Leske MC, et al. The prevalence of diabetic retinopathy among adults in the United States. Arch Ophthalmol. 2004; 122:552–563. [PubMed: 15078674]
- 36. Gepner AD, Young R, Delaney JA, et al. Comparison of coronary artery calcium presence, carotid plaque presence, and carotid intima-media thickness for cardiovascular disease prediction in the Multi-Ethnic Study of Atherosclerosis. Circ Cardiovasc Imaging. 2015; 8 pii: e002262.
- 37. Palmerini T, Biondi-Zoccai G, Riva DD, et al. Risk of stroke with percutaneous coronary intervention compared with on-pump and off-pump coronary artery bypass graft surgery: Evidence from a comprehensive network meta-analysis. Am Heart J. 2013; 165:910–917. e14. [PubMed: 23708161]
- 38. Mao Z, Zhong X, Yin J, et al. Predictors associated with stroke after coronary artery bypass grafting: a systematic review. J Neurol Sci. 2015; 357:1–7. [PubMed: 26208801]
- 39. Massaro A, Messe SR, Acker MA, et al. Pathogenesis and risk factors for cerebral infarct after surgical aortic valve replacement. Stroke. 2016; 47:2130–2132. [PubMed: 27382005]

- 40. Beach JM, Mihaljevic T, Svensson LG, et al. Coronary artery disease and outcomes of aortic valve replacement for severe aortic stenosis. J Am Coll Cardiol. 2013; 61:837–848. [PubMed: 23428216]
- Groom RC, Quinn RD, Lennon P, et al. Detection and elimination of microemboli related to cardiopulmonary bypass. Circ Cardiovasc Qual Outcomes. 2009; 2:191–198. [PubMed: 20031837]
- 42. Blauth C. Invited commentary. Ann Thorac Surg. 2011; 91:22–23. [PubMed: 21172478]
- DeFoe GR, Dame NA, Farrell MS, et al. Embolic activity during in vivo cardiopulmonary bypass. J Extra Corpor Technol. 2014; 46:150–156. [PubMed: 25208432]
- 44. Rodriguez RA, Nathan HJ, Ruel M, et al. A method to distinguish between gaseous and solid cerebral emboli in patients with prosthetic heart valves. Eur J Cardiothorac Surg. 2009; 35:89–95. [PubMed: 18952455]
- Rodriguez RA, Rubens FD, Wozny D, Nathan HJ. Cerebral emboli detected by transcranial Doppler during cardiopulmonary bypass are not correlated with postoperative cognitive deficits. Stroke. 2010; 41:2229–2235. [PubMed: 20724717]
- 46. Peretto G, Durante A, Limite LR, Cianflone D. Postoperative arrhythmias after cardiac surgery: incidence, risk factors, and therapeutic management. Cardiol Res Pract. 2014; 2014:615987. [PubMed: 24511410]
- Rhodes ET, Laffel LM, Gonzalez TV, Ludwig DS. Accuracy of administrative coding for type 2 diabetes in children, adolescents, and young adults. Diabetes Care. 2007; 30:141–143. [PubMed: 17192348]
- Park SJ, Choi NK, Seo KH, et al. Nationwide incidence of clinically diagnosed central retinal artery occlusion in Korea, 2008 to 2011. Ophthalmology. 2014; 121:1933–1938. [PubMed: 24913283]
- 49. Rudkin AK, Lee AW, Chen CS. Vascular risk factors for central retinal artery occlusion. Eye (Lond). 2010; 24:678–681. [PubMed: 19521436]

Incidence of Retinal Artery Occlusion among Patients Undergoing Cardiac Surgery in the National Inpatient Sample 1998–2013

Year	Affected with RAO	Total No. of Cardiac Surgeries	Incidence per 10 000 (95% CI)
1998	365	435 126	8.39 (6.64–10.76)
1999	359	414 628	8.65 (6.92–10.96)
2000	241	443 465	5.44 (4.18–7.23)
2001	230	451 122	5.11 (3.87-6.90)
2002	290	423 126	6.85 (5.36-8.88)
2003	272	413 322	6.57 (5.11-8.61)
2004	253	368 531	6.86 (5.26–9.11)
2005	206	344 026	5.98 (4.47-8.19)
2006	251	374 144	6.71 (5.16-8.91)
2007	249	317 194	7.84 (5.99–10.46)
2008	344	336 462	10.22 (8.17–12.97)
2009	333	355 773	9.37 (7.43–12.01)
2010	289	293 912	9.84 (7.67–12.85)
2011	267	300 103	8.90 (6.91–11.66)
2012	330	299 920	11.00 (8.70–14.14)
2013	285	301 980	9.44 (7.32–12.37)
1998–2013	4564	5 872 833	7.77 (7.29–8.29)

CI = confidence interval; RAO = retinal artery occlusion.

Results are national estimates using National Inpatient Sample (NIS) weighting and the Stata (StataCorp LP, College Station, TX) survey function. Respective 95% CIs appear in parentheses. See "Methods" for International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes.

Incidence of Retinal Artery Occlusion among Cardiac Surgical Procedures in the National Inpatient Sample from 1998 to 2013

Surgery Type	Affected with RAO	Total No. of Surgeries	Incidence per 10 000 (95% CI)
Atrial or ventricular septal surgeries	358	157 891	22.65 (18.12–28.70)
Left ventricular assist device	30	22 001	13.48 (6.16–35.61)
Total valve surgeries	1844	1 508 393	12.22 (11.07–13.54)
Pulmonary valve	20	13 991	14.39 (5.25–54.25)
Aortic valve	1307	1 018 054	12.84 (11.41–14.50)
Mitral valve	694	562 230	12.35 (10.51–14.61)
Tricuspid valve	55	56 788	9.61 (5.43–18.75)
Pericardiectomy	290	268 839	10.79 (8.41–14.07)
Operations on structures adjacent to heart valves	99	157 594	6.31 (4.16–10.05)
CABG	2781	4 616 746	6.02 (5.55-6.55)
Heart transplant	10	27 616	3.65 (0.79–36.72)

CABG = coronary artery bypass grafting; CI = confidence interval; RAO = retinal artery occlusion.

Results are national estimates using NIS weighting and the Stata survey function. Numbers are count estimates. See "Methods" for ICD-9-CM diagnostic codes. Results with n 10 could not be reported because of Agency for Healthcare Research and Quality privacy restrictions. The total number of RAO cases in the Table exceeds the total number among cardiac surgeries because of overlapping procedures.

Characteristics of All Cardiac Surgery Cases with and without Retinal Artery Occlusion in the National Inpatient Sample, 1998 to 2013

	All Cases: RAO	All Cases: Unaffected
All patients: No. of discharges	4564	5 868 269
Age group (yrs)		
18–30	51 (1.1%)	55 860 (1.0%)
31-40	150 (3.3%)	130 520 (2.2%)
41–50	440 (9.6%)	508 754 (8.7%)
51-60	937 (20.5%)	1 253 835 (21.4%)
61–70	1379 (30.2%)	1 752 873 (29.9%)
71–80	1288 (28.2%)	1 667 381 (28.4%)
>80	319 (7.0%)	499 046 (8.5%)
Missing	10(0.2%)	1123 (<0.1%)
Mean length of stay days (95% CI)	11.2 (10.5–11.8)	10.3 (10.1–10.4)
Mean total charges, \$ (95% CI; inflation adjusted to 2013)	149 338 (136 182–162 495)	131 776 (127 166–136 386
Gender (n = 5 871 578)		
Male	3157 (69.2%)	3 950 064 (67.3%)
Female	1406 (30.8%)	1 916 951 (32.7%)
Type of Admission ($n = 4\ 120\ 650$)		
Elective	1795 (53.4%)	2 134 492 (51.8%)
Nonelective	1564 (46.6%)	1 982 799 (48.2%)
Discharge Status		
Routine	2094 (45.9%)	2 961 080 (50.5%)
Short-term hospital	53 (1.2%)	50 651 (0.9%)
Home health care	1522 (33.4%)	1 667 511 (28.4%)
Other/missing	842 (18.5%)	979 919 (16.7%)
Died	52 (1.1%)	209 108 (3.6%)
Race		
White	3140 (68.8%)	3 698 062 (63.0%)
Black	146 (3.2%)	293 620 (5.0%)
Hispanic	174 (3.8%)	289 062 (4.9%)
Asian or Pacific Islander	39 (0.8%)	94 240 (1.6%)
Native American	18 (0.4%)	19 660 (0.3%)
Other	82 (1.8%)	147 841 (2.5%)
Missing	966 (21.2%)	1 325 784 (22.6%)
Acute coronary syndrome	567 (12.4%)	1 279 254 (21.8%)
Anemia	153 (3.4%)	175 898 (3.0%)
Aortic and mitral stenosis or insufficiency	283 (6.2%)	257 073 (4.4%)
Aortic stenosis or insufficiency	219 (4.8%)	102 764 (1.8%)
Atrial fibrillation	1372 (30.1%)	1 856 522 (31.6%)
Cardiogenic shock	120 (2.6%)	195 337 (3.3%)

	All Cases: RAO	All Cases: Unaffected
Cardiomyopathy	202 (4.4%)	283 773 (4.8%)
Carotid artery stenosis	893 (19.6%)	206 987 (3.5%)
Congestive heart failure	788 (17.3%)	1 305 185 (22.2%)
Coronary artery disease	3136 (68.7%)	4 799 368 (81.8%)
DM type 1 without complications	33 (0.7%)	95 684 (1.6%)
DM type 2 without complications	784 (17.2%)	1 400 061 (23.9%)
DM with neurologic manifestations	55 (1.2%)	106 531 (1.8%)
DM with ophthalmic manifestations	70 (1.5%)	68 885 (1.2%)
DM with renal manifestations	21 (0.4%)	74 022 (1.3%)
Giant cell arteritis	19 (0.4%)	3215 (<0.1%)
Hypercoagulable state	48 (1.1%)	13 653 (0.2%)
Hyperlipidemia	2136 (46.8%)	2 741 866 (46.7%)
Hypertension	2485 (54.4%)	3 245 676 (55.3%)
Hypertension with cardiac complications	72 (1.5%)	92 040 (1.6%)
Intra-aortic balloon pump	228 (5.0%)	456 652 (7.8%)
Mitral stenosis or insufficiency	77 (1.7%)	62 974 (1.1%)
Myxoma	73 (1.6%)	22 636 (0.4%)
Obesity	395 (8.6%)	645 867 (11.0%)
Peripheral vascular disease	306 (6.7%)	284 291 (4.8%)
Postoperative bleed	1041 (22.8%)	1 034 359 (17.6%)
Smoking	1076 (23.6%)	1 554 047 (26.5%)
Stroke	541 (11.9%)	153 927 (2.6%)
Thrombocytopenia	408 (8.9%)	535 130 (9.1%)
Transfusion	1209 (26.5%)	1 335 355 (22.8%)
Ventricular septal defect	10(0.2%)	9674 (0.2%)

CI = confidence interval; DM = diabetes mellitus; RAO = retinal artery occlusion.

Results are national estimates using NIS weighting and the Stata survey function. Numbers are count estimates or means with % (parentheses) and respective 95% CIs in parentheses when indicated. Results with n 10 could not be reported because of Agency for Healthcare Research and Quality privacy restrictions. See "Methods" for ICD-9-CM diagnostic codes. Total charges (USD) were inflation adjusted to 2013 with Bureau of Labor Statistics (http://www.bls.gov/data/).

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Multivariable Analysis for Retinal Artery Occlusion and Cardiac Surgery in the National Inpatient Sample, 1998 to 2013

Covariate	OR (95%CI)	P Value	VIF
Acute coronary syndrome	0.72 (0.58–0.89)	0.003	1.21
Aortic insufficiency	1.85 (1.26–2.71)	0.002	1.10
Atrial fibrillation	0.82 (0.70-0.95)	0.01	1.16
Carotid stenosis	7.52 (6.22–9.09)	< 0.001	1.02
Congestive heart failure	0.73 (0.60-0.88)	< 0.001	1.16
DM type 2	0.74 (0.61–0.89)	0.001	1.10
DM with ophthalmic complications	1.89 (1.10–3.24)	0.02	1.10
Embolic stroke	4.43 (3.05–6.42)	< 0.001	1.08
Female gender	0.77 (0.66–0.89)	< 0.001	1.08
Giant cell arteritis	7.73 (2.78–21.52)	< 0.001	1.00
Hypercoagulable state	2.90 (1.56-5.39)	< 0.001	1.00
Myxoma	2.43 (1.39-4.26)	0.002	1.07
Smoking	0.82 (0.70-0.97)	0.02	1.10
Transient cerebral ischemia	7.67 (5.31–11.07)	< 0.001	1.00
Thrombocytopenia	0.79 (0.62–1.00)	0.049	1.08
Postoperative bleed	1.34 (1.13–1.58)	0.001	1.07
Aortic valve surgery	1.58 (1.29–1.95)	< 0.001	1.63
CABG	0.61 (0.48–0.79)	< 0.001	3.03
Mitral valve surgery	1.68 (1.34–2.10)	< 0.001	1.42
Septal surgery	2.16 (1.62–2.87)	< 0.001	1.15

CABG = coronary artery bypass grafting; CI = confidence interval; DM = diabetes mellitus; VIF = variance inflation factor (<10 indicates no collinearity).

Race was not a significant risk factor for RAO. Only statistically significant (P < 0.05) covariates are shown. Results of nonsignificant covariates are shown in Table S3 (available at www.aaojournal.org). The multivariate model includes patients undergoing multiple procedures (i.e., a patient could undergo CABG and valve surgery, which would be considered as 2 different procedures). Thus, a separate model was run eliminating patients undergoing multiple procedures (i.e., the single procedure model). The results (not shown) were similar to those of this model (see "Results" section).