Risk factors for central retinal artery occlusion in young patients

The acute irreversible loss of vision associated with central retinal artery occlusion (CRAO) can be devastating, especially in young patients. The literature has revealed potential risk factors, including hypercoagulability, trauma, sickle cell disorders, cardiac valvular disease, carotid stenosis, use of oral contraceptives, pregnancy, collagen vascular disease, increased intraocular pressure, optic nerve drusen, congenital prepapillary arterial loop, intravenous drug abuse, migraine, vasculitis, and perioperative factors in young patients with CRAO.[1–3] This retrospective case-control study aims to evaluate systemic and ocular comorbidities associated with CRAO in young patients.

This study was performed using data from the 2002–2014 National Inpatient Sample (NIS) Database.[4,5] Cases included 522 (weighted) hospitalized young adults between the ages of 20 and 45 years with an admitting diagnosis of acute CRAO, and controls, matched by age and sex, were 5430 (weighted) individuals who did not have any diagnosis of retinal artery occlusion. The average age of subjects in the CRAO and non-CRAO cohorts was 37.3 and 37.4 years, respectively ($p = 0.800$). Men constituted 58.4% and 56.6% of the non-CRAO and CRAO cohorts, respectively ($p = 0.400$). The ethnic background of the CRAO cases versus controls included White participants 42.1% versus 55.9% ($p < 0.001$), Black participants 28.1% versus 8.2% ($p < 0.001$), Hispanic participants 4.5% versus 25.6% ($p < 0.001$), Asian/Pacific Islander participants 4.7% versus 2.0% ($p < 0.001$), and Native American participants 0% versus 6.9% ($p < 0.001$).

A higher prevalence of certain systemic comorbidities was noted in CRAO cases compared with controls (Table 1); these comorbidities included hypertension 41.4% versus 23.3%, tobacco use 32.3% versus 23.7%, hyperlipidemia 21.0 versus 9.2, cardiac valvular disease 9.6 versus 2.2, and migraine 6.7 versus 2.7. Carotid stenosis, history of cerebral stroke, sickle cell disease, atherosclerosis, and aortic disease/aneurysm were significantly more prevalent in CRAO cases. Acute thromboembolic events were reported during hospitalization of CRAO patients and included Deep Vein Thrombosis or Pulmonary Embolism (4.7%), ischemic stroke (4.0%), and Transient Ischemic Attack (1.1%). Furthermore, 9.6% of cases underwent cerebral angiography, and 29.1% echocardiography. No patients underwent endarterectomy, and no in-hospital deaths were reported. The length of hospitalization varied significantly between cases and controls (3.45 days vs 4.29 days; $p < 0.001$), and no significant difference was found in the hospital cost per day between the cases and controls ($9964 vs $9283; $p = 0.083$).

Table 1—Comparison of patients with and without CRAO

Variable	Controls (n = 5430)		Cases (n = 522)		p
	Count	%	Count	%	
Age					
Average age (y)	37.30		37.38		0.800
Age group (y)					0.566
20–29	1055	19.40	96	18.40	
30–45	4375	80.60	426	81.60	
Sex					0.400
Men	3172	58.40	295	56.60	
Women	2258	41.60	227	43.40	
Ethnicity					
White	3033	55.90	220	42.10	<0.001
Black	444	8.20	147	28.10	<0.001
Hispanic	1391	25.60	24	4.50	<0.001
Asian/Pacific Islander	108	2.00	25	4.70	<0.001
Native American	377	6.90	0	0.00	<0.001
Other	5	0.10	30	3.90	<0.001
Systemic comorbidities					
Aortic dissection aneurysm	5	0.10	10	1.90	<0.001
Atherosclerosis	32	0.60	10	1.90	0.001
Atrial fibrillation/flutter	115	2.10	5	1.00	0.072
Carotid dissection	5	0.10	0	0.00	0.488
Carotid stenosis	5	0.10	30	5.80	<0.001
Cocaine use	101	1.90	5	0.90	0.137
Bleeding diathesis	199	3.70	20	3.90	0.814
Congestive heart failure	89	1.60	14	2.80	0.076
DVT/PE (history)	157	2.90	25	4.70	0.017
Diabetes with chronic complications	162	3.00	14	2.80	0.719
Diabetes without chronic complications	529	9.70	29	5.60	0.002
Intravenous drug use	110	2.00	5	0.90	0.094
Hyperlipidemia	501	9.20	109	21.00	<0.001

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Table 1—*Continued*

Variable	Controls (n = 5430)		Cases (n = 522)		*p*
	Count	%	Count	%	
Primary hypercoagulable state	19	0.30	25	4.90	<0.001
Hypertension	1267	23.30	214	41.40	<0.001
Leukemia	63	1.20	0	0.00	0.013
Non-Hodgkin lymphoma	29	0.50	0	0.00	0.094
Migraine	149	2.70	35	6.70	<0.001
Obesity	498	9.20	60	11.50	0.072
Pregnancy	14	0.30	0	0.00	0.245
Pseudotumour cerebri	10	0.20	0	0.00	0.326
Rheumatoid arthritis/collagen vascular diseases	71	1.30	4	0.90	0.299
Sickle cell disease trait	43	0.80	9	1.80	0.029
Stroke (history)	43	0.80	19	3.70	<0.001
Syphilis	10	0.20	9	1.80	<0.001
Systemic vasculitides	0	0.00	5	0.90	<0.001
Tobacco use	1288	23.70	169	32.30	<0.001
Cardiac valve disease	120	2.20	50	9.60	<0.001
Glaucoma with NVG	4	0.10	10	1.80	<0.001
In-hospital complications					
DVT/PE (acute)	211	3.90	25	4.70	0.317
Myocardial infarction (acute)	43	0.80	0	0.00	0.041
Ischemic stroke	5	0.10	21	4.00	<0.001
Hemorrhagic stroke	10	0.20	0	0.00	0.326
Transient ischemic attack	19	0.40	6	1.10	0.007
Systemic venous thrombosis	52	1.00	13	2.50	0.001
In-hospital procedures					
Cerebral angiography	44	0.80	50	9.60	<0.001
Carotid ultrasound	0	0.00	15	2.80	<0.001
Echocardiography	48	0.90	152	29.10	<0.001
Medication					
Anticoagulation	122	2.30	30	5.70	<0.001
Antiplatelet	14	0.30	0	0.00	0.245
Aspirin	59	1.10	4	0.80	0.495
Hospital course					
Mean length of stay (days)	4.29		3.45		<0.001
Mean cost per day (dollars)	9283		9964		0.083
Died during hospitalization	19	0.40	0	0.00	0.176

DVT = Deep Vein Thrombosis. PE = Pulmonary Embolism.

Comorbidities that significantly increased the risk of CRAO included systemic vasculitides (Odds Ratio (OR) = 164.68), carotid stenosis (OR = 61.66), glaucoma (OR = 26.48), hypercoagulable state (OR = 14.82), syphilis (OR = 5.40), cardiac valve disease (OR = 3.36), migraine (OR = 3.14), and hypertension (OR = 1.97) (Table 2).

Recent evidence suggests that cerebrovascular accidents may occur within a month of acute CRAO in up to 25% of cases; the American Heart Association and American Academy of Ophthalmology recommend that, irrespective of age, all of these patients should undergo urgent stroke work-up.[6] This study showed that a myriad of systemic conditions and glaucoma are risk factors for acute CRAO in young adults.

Because the present study uses a national database, it is retrospective in nature, and one cannot determine causality.

Table 2—Results of regression analysis

Variable	Univariable	*p*	Multivariable	*p**
Age group (y)				
20–29	1.00	Ref	1.00	Ref
30–45	1.06 (0.84–1.34)	0.597	—	—
Sex				
Women	1.00	Ref		
Men	1.08 (0.90–1.29)	0.413	—	—
Ethnicity				
White	1.00	Ref		
Black	4.39 (3.54–5.44)	<0.001	3.56 (2.77–4.56)	<0.001
Hispanic	0.14 (0.09–0.21)	<0.001	0.23 (0.15–0.36)	<0.001
Asian/Pacific Islander	2.47 (1.58–3.86)	<0.001	2.86 (1.78–4.59)	<0.001
Native American	0.01 (0.00–0.21)	<0.001	0.02 (0.00–0.35)	0.007
Other	40.93 (15.55–107.71)	<0.001	50.67 (18.96–135.4)	<0.001
Systemic comorbidities				
Aortic dissection aneurysm	19.92 (6.75–58.81)	<0.001	4.55 (1.07–19.41)	0.041
Atherosclerosis	3.38 (1.65–6.91)	<0.001	3.06 (1.20–7.76)	0.019
Atrial fibrillation flutter	0.49 (0.21–1.16)	0.106	—	—

(*continued*)

Table 2—*Continued*

Variable	Univariable	*p*	Multivariable	*p**
Carotid dissection	0.96 (0.04–23.12)	0.980	—	—
Carotid stenosis	62.86 (24.76–159.61)	<0.001	61.66 (23.83–159.54)	<0.001
Bleeding diathesis	1.10 (0.70–1.75)	0.678	—	—
Congestive heart failure	1.76 (1.00–3.07)	0.048	1.19 (0.64–2.19)	0.584
DVT/PE (history)	1.68 (1.09–2.59)	0.019	0.65 (0.36–1.17)	0.147
Diabetes with chronic complications	0.96 (0.56–1.64)	0.870	—	—
Diabetes without chronic complications	0.56 (0.38–0.82)	0.003	0.44 (0.29–0.69)	<0.001
Intravenous drug use	0.47 (0.19–1.17)	0.104	—	—
Hyperlipidemia	2.61 (2.08–3.29)	<0.001	1.37 (1.02–1.84)	0.035
Primary hypercoagulable state	14.5 (7.94–26.47)	<0.001	14.82 (6.52–33.71)	<0.001
Hypertension	2.32 (1.93–2.79)	<0.001	1.97 (1.58–2.46)	<0.001
Leukemia	0.08 (0.00–1.34)	0.079	—	—
Non-Hodgkin lymphoma	0.17 (0.01–2.97)	0.227	—	—
Migraine without cerebral infarction	2.56 (1.75–3.74)	<0.001	3.14 (2.04–4.82)	<0.001
Obesity	1.30 (0.97–1.72)	0.075	—	—
Peripheral artery disease	2.97 (1.80–4.89)	<0.001	0.42 (0.18–0.99)	0.048
Pregnancy	0.36 (0.02–6.59)	0.488	—	—
Pseudotumour cerebri	0.50 (0.03–9.92)	0.652	—	—
Rheumatoid arthritis	0.72 (0.29–1.82)	0.492	—	—
Sickle cell disease trait	2.35 (1.16–4.75)	0.018	0.35 (0.13–0.97)	0.044
Stroke (history)	4.87 (2.83–8.38)	<0.001	2.20 (1.11–4.34)	0.024
Syphilis	10.24 (4.16–25.17)	<0.001	5.40 (1.89–15.45)	0.002
Systemic vasculitides	108.98 (4.45–2666.38)	0.04	164.68 (5.60–4846.00)	0.003
Tobacco use	1.54 (1.27–1.87)	<0.001	1.21 (0.97–1.52)	0.088
Cardiac valve disease	4.73 (3.36–6.66)	<0.001	3.36 (2.19–5.16)	<0.001
Glaucoma (includes neovascular glaucoma)	23.27 (7.35–73.66)	<0.001	26.48 (7.95–88.19)	<0.001

DVT = Deep Vein Thrombosis. PE = Pulmonary Embolism.
*Bonferroni correction: $p = 0.003$.

Furthermore, the accuracy of the analysis depends on the accuracy of the health care providers coding the diagnoses. These limitations are not unique to this database or study. Additionally, although the control group was matched by sex and age, it was not matched by ethnicity, which may introduce variation; however, the variation is likely modest and unlikely to affect the regression analysis, which includes ethnicity. Lastly, because the cases and controls of this study are inpatients, there is likely to be a higher prevalence of chronic conditions requiring multiple hospitalizations than what would be seen in a study of outpatients.

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Footnotes and Disclosure

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