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REVIEW

Is a Carotid Doppler Scan Useful for Managing Patients with Suspected Ocular Ischemic Syndrome?

Anastasia Gkiala, Naima Zaheer, Saba Anwar, Shalika Perera, Ahmad Sharara, Peck Lin Lip

Birmingham & Midland Eye Centre, Sandwell & West Birmingham NHS Trust, City Hospital, Birmingham, B18 7QH, UK

Correspondence: Peck Lin Lip, Birmingham & Midland Eye Centre, City Hospital, Dudley Road, Birmingham, B18 7QH, UK, Tel +44 121 5543801, Fax +44 121 5076791, Email pllipwoo@gmail.com

Purpose: This review aims to understand the value of a carotid Doppler scan (CDS) when managing patients with clinical/suspected ocular ischaemic syndrome (OIS); correlations between internal carotid artery (ICA) stenosis reports; subsequent patterns of referral to vascular experts; and subsequent decisions concerning surgical versus medical management.

Methods: A retrospective review of 402 CDS requests by a single eye center over 4 years (2016–2019) for patients with a clinical suspicion of OIS was conducted. Data analysis included 344 patients who had reported CDS of both ICAs. We also studied referral patterns by ophthalmologists to other specialties.

Results: CDS requests were related to the retina (53.2%), neuro/TIA problems (31.1%), glaucoma (10.5%) and other issues (5.2%). The majority of patients (209/344, 60.8%) had normal CDA results. Of the 688 ICAs reported, 469 (68.2%) were normal, 219 (31.8%) had atheroma present, and only 83 (12.1%) had significant stenosis. Of 83 ICAs with stenosis, 23 (27.7%) had ≥70% stenosis, 24 (28.9%) had 50–69% stenosis, and 25 (30.1%) had <50% stenosis. A total of 60/344 (17.4%) patients were referred to vascular/stroke teams: 15/60 (25%) referred had bilateral disease, and only 2/60 (3.3%) were offered carotid endarterectomy. All referred patients commenced statins and low-dose aspirin.

Conclusion: Our cohort showed a low incidence of ICA stenosis according to CDS reports in patients with suspected OIS. There were very low rates of vascular and endarterectomy referral. Commencement of conservative treatment (mini aspirin+statin) by ophthalmologists could be beneficial even in the early stage of presenting clinical evidence of OIS.

Plain Language Summary: Ocular ischemic syndrome (OIS) covers a wide spectrum of eye problems resulting from reduced blood flow to the eyes. OIS is commonly known to be a rapidly blinding disease due to late diagnosis. A high index of suspicion can lead to early investigation and perhaps prevent blindness with timely intervention. The fluorescein angiogram is a reliable eye test to confirm OIS disease affecting the retina. If reduced retina perfusion is confirmed, a carotid Doppler artery scan (CDS) is the next investigation to detect blood vessel lumen narrowing primarily affecting carotid arteries (neck arteries). The presence of carotid artery disease can indicate risk of stroke; hence, confirmed carotid artery disease merits a referral to vascular surgeons to consider carotid artery surgery aiming to unblock the artery and improve blood flow and hopefully reverse OIS.

Our study aimed to investigate the prevalence of suspected OIS patients referred for carotid Doppler scans, correlations between carotid artery stenosis results and clinical OIS, and subsequent offers of carotid artery surgery versus conservative medical management.

Our study showed that carotid artery disease severity defined by CDS has a poor correlation with clinical diagnosis of OIS. Conservative treatment is advised for all patients with carotid artery disease, whereas surgical options for carotid stenosis are rarely offered. Hence, this study questions the benefit of pursuing CDS tests in OIS patients, since the results do not change their management. Finally, we highlight the need for better guidance on carotid artery stenosis referral for carotid surgery.

Keywords: carotid endarterectomy, internal carotid arteries, stenosis, medical treatment

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Introduction

Ocular ischemic syndrome (OIS) is a wide term describing ocular dysfunctions resulting from ocular hypoperfusion. The commonest OIS manifestations are in the posterior segment of the eye, often as detectable peripheral retinal haemorrhages, as venous-stasis retinopathy, retinal artery/vein occlusions, ischemic optic neuropathy, asymmetrical diabetic retinopathy, etc. The most severe OIS manifestations are retinal/iris neovascularizations and vitreous haemorrhage from untreated underlying OIS-related retinal ischaemia. Less frequently, it can also be associated with anterior segment diseases such as unresolving corneal disease (unresolving and chronic poor healing corneal ulcer) and normal tension glaucoma. Generally, OIS diagnosis requires a higher index of suspicion than other differential diagnoses.[1–4]

OIS is primarily due to ipsilateral carotid artery disease, attributed to atheromatous narrowing of vessel lumen compromising ocular microcirculation. When OIS is clinically suspected, a duplex Doppler ultrasonography (namely, a carotid Doppler scan [CDS]) of the carotid arteries is usually carried out, combining B-mode ultrasonography and a Doppler scan for assessing blood flow velocity and vessel lumen diameter.[5] CDS is an easily accessible investigation, a non-invasive procedure that provides reliable information on lumen health for larger carotid arteries, common carotid artery (CCA), internal and external carotid arteries (ICA, ECA); however, it is unable to delineate smaller vessel pathologies of the ophthalmic artery and posterior ciliary arteries.

Management options for OIS include treatment of the presenting ocular disease as well as surgical intervention such as carotid artery endarterectomy (CEA) for any significant carotid stenosis. Historic indications for CEA are severe artery stenosis (70–99%) and sometimes moderate stenosis (30–69%) but not mild artery disease.[6] However, the CEA option is not commonly offered, as the guidance for CEA is far from clear when considering the common complex medical diseases of individual patients. In particular, CEA for eye disease spectra arbitrarily included only definite visual loss resulting from central retinal artery occlusion or amaurosis fugax. For patients with confirmed carotid artery disease with or without a CEA surgical option, conservative medical treatment, such as prescribing aspirin and statins, has been the standard recommendation for lowering systemic vascular risk factors.[6,7]

Published literature indicated that OIS incidence is relatively rare, with an estimated occurrence of 7.5 cases/year/million people.[1] We believe this is an underestimation due to the low diagnostic index of suspicion that means OIS is under-investigated. Our study aims to understand the value of CDS as an investigative tool in managing OIS or clinically suspected OIS patients, subsequent referral patterns to vascular experts and their decision outcomes on CEA versus medical management of these patients.

Methods

Study Design

Our study involved retrospective data collection and analysis of the results of OIS patients who were referred for carotid Doppler scans (CDSs) at a single hospital over a 4-year period (2016–2019). Our OIS cohort primarily included clinically-established OIS from medical retina specialists (fundus fluorescein angiogram confirmed retinal non-perfusion of OIS pattern), and also clinically-suspicious OIS from all other eye subspecialties. The referral for a CDS could involve one affected eye or both eyes.

A total of 402 requests for a CDS were made to our eye center over the 4-year period analyzed. Of these, 58 patients were excluded from the analysis because no CDS results were available as a result of patients' non-attendance, hospital cancellations or unavailability of reports.

Data Collection

A total of 344 patients' data were available for analysis. All data were obtained from patients' electronic medical records. Data of interest included patients' age, gender, referral category by eye subspecialties and laterality of clinically affected eye.

The CDA analyses were based on radiologists' reports on internal carotid artery (ICA) disease for each eye, describing the degree of atheroma presence/stenosis significance and corresponding flow velocity. We also included

data on subsequent referrals to vascular surgeons or the stroke team for patients with reported carotid artery stenosis, and subsequent decision outcomes of surgical versus conservative interventions.

Ethics and Data Analysis

This retrospective study was conducted at Birmingham & Midland Eye Centre, Birmingham, UK, and received ethical approval from the Institutional Review Board (Sandwell and West Birmingham Research and Development review board) in accordance with UK "Good Clinical Practice" regulations. It also adhered to the tenets of the Declaration of Helsinki. Informed written consent was obtained from all patients who had undergone invasive investigation or treatment procedures as part of routine and standard clinical care in our real-world clinical practice. Descriptive statistics were used to show demographic and baseline characteristics. Statistical analyses were performed using Microsoft Excel 2016 for Windows and SSPS Statistics (IBM Corp., Armonk, USA).

Results

Of the 344 patients with clinically suspected OIS who had CDA reports, 155 were female and 189 were male, with an average age of 65 years (SD 14.63, range 19–101). The majority of CDA referrals were made in relation to medical retina problems (53.2%), followed by neuro-ophthalmology/transient ischemic attack (TIA) (31.1%) and glaucoma (10.5%). Other specialties, such as oculoplastics, cornea and uveitis, accounted for 5.2% of referrals (Figure 1).

Data Analysis Based on Number of Patients (n=344)

The clinically affected eye was the right eye for 136 patients (39.5%); the left eye accounted for 124 patients (36%); and 84 patients (24.4%) had bilateral involvement. A total of 209 patients (209/344, 60.8%) had a CDA result showing completely normal ICA. Presence of atheroma was reported as a unilateral disease in 51 patients (51/344, 14.8%) and a bilateral disease in 84 patients (84/344, 24.4%). Furthermore, all patients diagnosed with bilateral OIS had atheroma

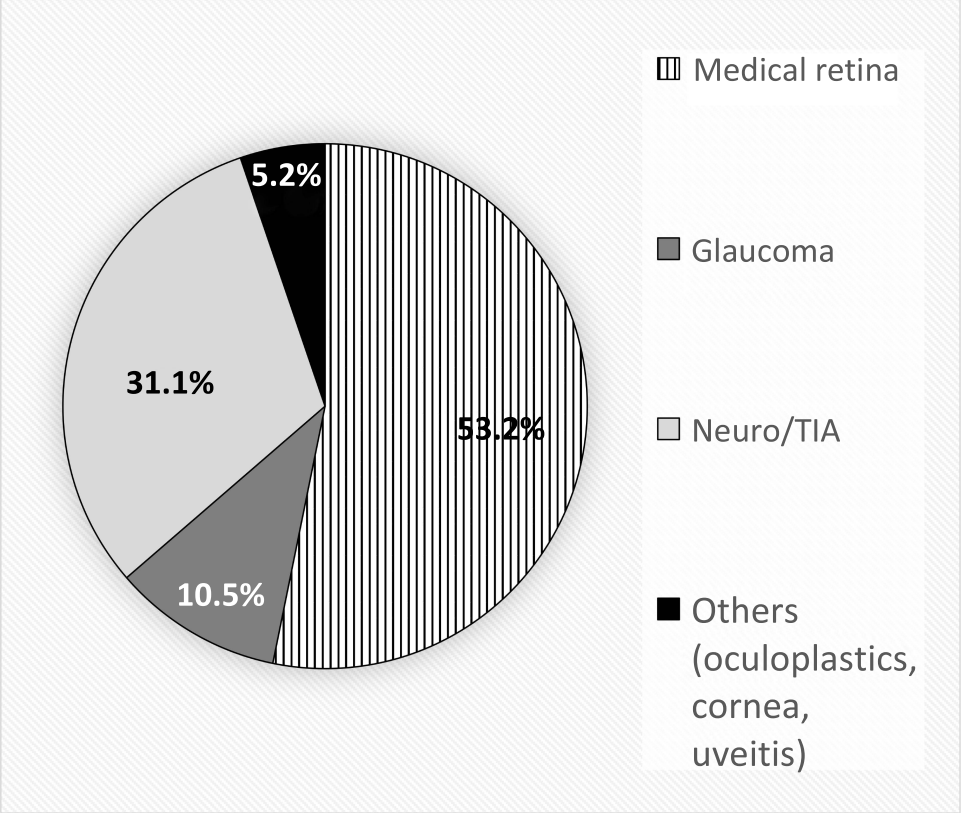

Figure 1 Pattern of referrals for carotid Doppler scan by different eye subspecialties (n=344).

present in both ICAs except 10 patients (who had atheroma present in only one eye). Eleven unilateral OIS patients had atheroma reported in their contralateral eye (no atheroma in the ipsilateral eye) and 55 unilateral OIS patients had atheroma detected in both their ICAs.

Data Analysis Based on Number of Eyes (n=688)

CDA reports for a total of 688 eyes (of 344 patients) were analyzed: 469 eyes (469/688, 68.2%) were reported to have normal ICA, while the presence of atheroma (of any degree) in ICA was mentioned in 219 eyes (219/688, 31.8%) (Figure 2A and Table 1). From the 219 eyes with atheroma, 136 (136/219, 62.1%) were reported to have no significant ICA stenosis, while 83 eyes (83/219, 37.9%) were reported to have varying percentages of stenosis present (Figure 2A and Table 1). The degrees of reported ICA stenosis severity were categorized into <50% stenosis, 50–69% stenosis, and ≥70% stenosis. The majority of reported ICA stenosis cases were in the less than 70% stenosis category (49/83, 59%), with only 27.7% (23/83) in the ≥70% stenosis category (Figure 2B), which was the stenosis category deemed suitable for referral to a vascular surgeon for consideration of CEA.

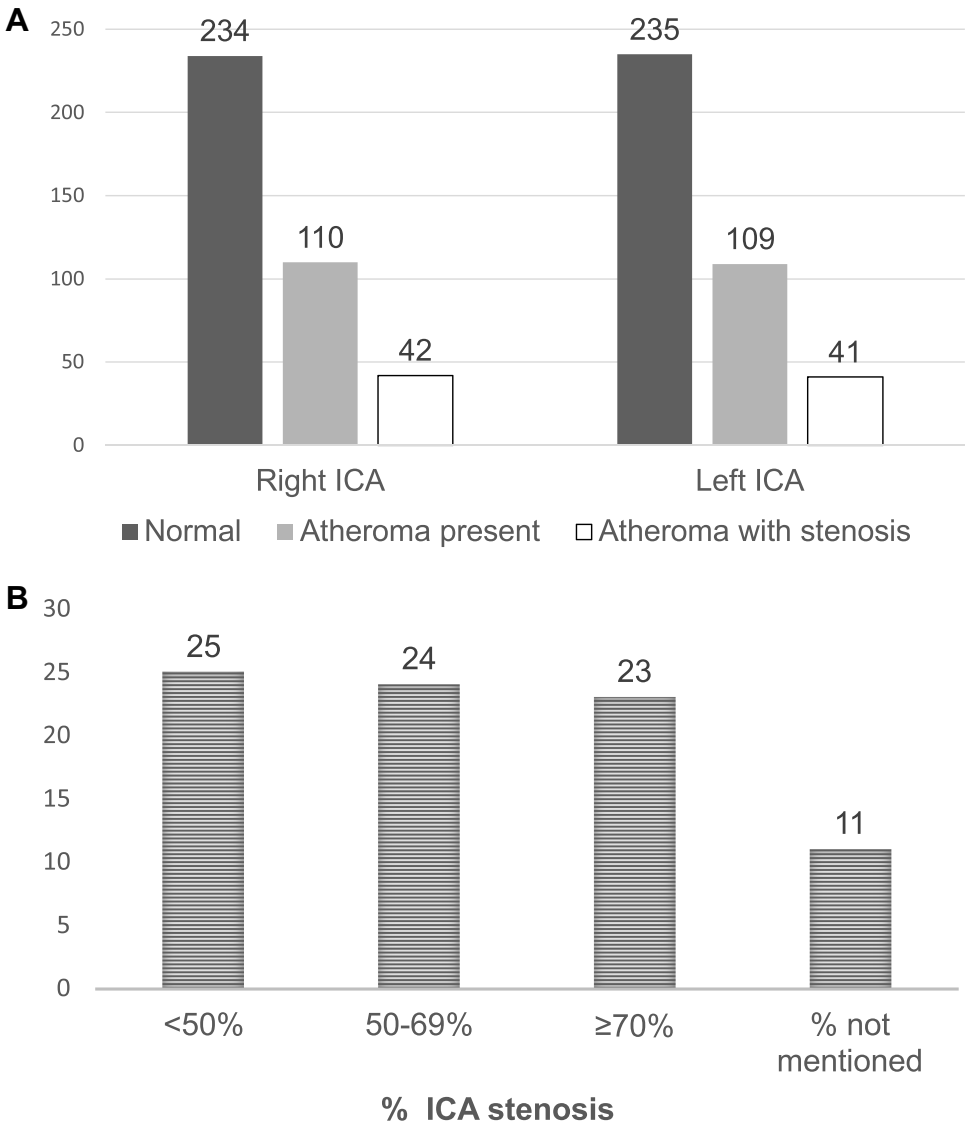

Figure 2 (**A**) Carotid Doppler scan reports on the presence of atheroma and stenosis of internal carotid arteries (n=688). (**B**) Reported carotid Doppler scans on ICA stenosis severities in percentage categories (n=83). Only 27.7% (23/83) reported stenosis in the ≥70% category.

Table 1 Carotid Doppler Reports on Internal Carotid Arteries, n=688

Carotid Doppler Report	Right ICA	Left ICA	N=688 (%)
Normal	234	235	469 (68.2%)
Atheroma present	110	109	219 (31.8%)
Subgroup 1: atheroma without stenosis	68	68	136 (19.8%) (136/219, 62.1%)
Subgroup 2: atheroma with stenosis	42	41	83 (12.1%) (83/219, 37.9%)

Based on the CDA reports, a total of 60 patients (60/344, 17.4%) with ICA stenosis were subsequently referred to either vascular surgeons (20 patients, 5.8%) or the stroke team (40 patients, 11.6%) (Figure 3A). All patients referred to vascular surgeons had at least one ICA with significant stenosis ≥70%. Most patients with a degree of stenosis less than 70% were referred to stroke physicians, with 77.5% (31/40 patients) in the stroke referral group also having significant stenosis ≥70%. Bilateral ICA stenosis disease constituted 50% of vascular surgeon referrals and 12.5% of stroke team referrals. From the total of 20 patients referred to the vascular team, only 2 patients (2/20, 10%) were offered endarterectomy (Figure 3B), while all of them (100%) were offered medical treatment (low-dose aspirin and statins).

Discussion

The use of CDS in investigating OIS has been common practice since internal carotid artery stenosis was identified as potentially the most common cause of ocular hypoperfusion. Mizener et al reported that 74% of their cohort with clinically evident OIS had occlusion or severe stenosis of the internal carotid artery (80–99%).[8] However, the low percentage of detection of clinically significant carotid stenosis in our cohort suggests that an alternative mechanism of ocular hypoperfusion might be present, which puts the usefulness of CDS under question. This low percentage could be attributed to the fact that CDS is only useful in detecting larger arterial stenosis (the carotid arteries), while reduced ocular perfusion leading to OIS could be a result of stenosis of other smaller artery vessels (ophthalmic artery, posterior ciliary arteries) that are not accessible by CDS.

Ghoraba et al described two cases of clinically evident OIS but negative CDS where stenosis of the aortic arch vessels and ophthalmic artery was detected by computed tomography angiogram (CTA) and magnetic resonance angiography (MRA), respectively. The signs of the former were completely resolved after common carotid angioplasty and stenting.[9] The impact of ophthalmic artery stenosis that cannot be detected by regular Doppler ultrasonography but is evident on Color Doppler imaging (CDI) was also described by Costa et al. The involvement of the ophthalmic arteries and use of specific Doppler imaging on proximal ocular blood vessel disease in the detection of stenosis of relevant arteries is also supported by multiple other studies.[10–12] In terms of practicality, the use of this specific diagnostic modality is limited due to the requirement of the specific skills of a trained imaging operator and, hence, low reproducibility of findings and low availability of the test/tool.[10,13]

Mendrinos et al suggested that the presence of collateral vessels between the internal and external carotid arteries helps to maintain ocular perfusion even with almost complete occlusion of the ICA.[2] In contrast, a poorly developed collateral system can progress to ocular ischemia even with ICA occlusion of less than 50%.[8] This group of patients usually presents with concurrent neurologic pathologies, such as cerebral infarction.[2] In the absence of collateral vessels and a proximal ICA obstruction, the ophthalmic artery shunts blood away from the eye, towards the circle of Willis, acting as a communication between the ECA and the distal, patent ICA. This is referred to as the "steal phenomenon". When collateral vessels are present, the shunt occurs through them, and an anterograde flow is noted in Doppler flowmetry.[10] This pathophysiological phenomenon could explain why the majority of carotid Doppler results were reported as insignificant stenosis in our OIS cohort.

Our study findings are in agreement with the above literature suggesting that OIS can present with normal or insignificant CDS findings. We suggest that a high level of clinical suspicion should be maintained. OIS is a rapidly blinding disease associated with a significant risk of cerebrovascular, ocular, and systemic morbidity, so prompt initiation of management is strongly advised.[14] This includes targeted treatment of the clinical presentation, for example pan retinal photocoagulation in cases of retinal neovascularization or administration of anti-VEGF in cases of iris neovascularization

Figure 3 (**A**) Pattern of referrals to vascular/stroke teams for patients after carotid Doppler scan results (n=344). A total of 60 patients (60/344, 17.4%) with reported internal carotid artery stenosis were referred to either vascular surgeons (20 patients, 5.8%) or the stroke team (40 patients, 11.6%). (**B**) Number of patients offered carotid artery endarterectomy following referral to a vascular surgeon was 10% (2/20 patients).

and neovascular glaucoma. A complete systemic workup, optimization of cardiovascular risk factors, namely hypertension, diabetes and hypercholesterolemia, identifying clotting and smoking status, and timely initiation of statins and aspirin is needed.[4,15] Whilst the vascular/stroke team advised all patients on statins and mini/low-dose aspirin, it is not illogical for ophthalmic specialists to follow the advice earlier for patients with established or clinical suspicion of ocular hypoperfusion even when the CDA report shows no significant carotid stenosis. When there is suspicion of proximal

ocular blood vessel disease causing ocular ischemia, it is our duty to understand the "undetectable but likely existing disease" and implement the benefits to prevent the risk of bilateral disease.

The North American Symptomatic Carotid Endarterectomy Trial found that carotid endarterectomy (CEA) was superior to medical management alone in the setting of perioperative stroke and death.[16] However, to our knowledge there is no published literature comparing surgical versus lone medical management for patients with clinically evident OIS. In cases where significant carotid artery stenosis is indeed detected by CDS, a referral to the vascular surgery team should be made for the consideration of surgical intervention such as carotid endarterectomy (CEA) or stenting (CAS). Many authors reported improvement and even complete reversal of the ocular symptoms after surgery. In a study conducted by Neroev et al, a total of 113 patients with OIS underwent CEA. The study found a 16% improvement in visual acuity in patients who had received surgery, as well as improvements in visual fields and electrophysiological characteristics.[17] These findings are supported by further, smaller studies.[18,19] However, carotid artery interventions (CEA, CAS) in the setting of OIS have been associated with severe complications. Few studies describe acute neovascular glaucoma after CEA, due to the imbalance between immediate recovery of aqueous production without an equal recovery of aqueous drainage.[20–22] Hyperperfusion syndrome post CEA and CAS has also been established.[23]

In our study, a low percentage of surgical interventions was observed. This could be attributed to the multiple eligibility criteria of this high-risk procedure such as stenosis degree, contralateral artery occlusion, patient life expectancy, stroke risk, availability of a vascular surgeon, and pre-operative classification of procedure risk.[24,25] The very small percentage of surgical interventions offered in our cohort was based on a CDS result of >70% stenosis because the available CEA guidance regarding ophthalmic patients was thus far restricted to manifested central retinal artery occlusion and amaurosis fugax. To stress this, referrals of asymptomatic patients with evident retinal hypoperfusion would be considered ineligible for vascular referral/consideration for CEA, regardless of the fact that their CDAs reveal significant ICA stenosis. In most cases, by the time significant stenosis is evident on CDA and thus warrants surgical intervention, irreversible ischemic damage has already happened in the eye. Future studies need to be conducted in order to prove the potential benefit of surgical intervention guided by clinical signs of ocular ischemia even before significant stenosis is detected on Doppler scanning.

Conclusion

Ocular ischemic syndrome can have significant and sight-threatening ocular manifestations. Our cohort showed that, despite manifestations of ocular hypoperfusion, there is poor correlation with carotid Doppler ultrasonography results for internal carotid artery disease.

Our cohort puts the usefulness of carotid Doppler ultrasonography as a diagnostic tool for patients with clinically evident OIS under question, suggesting it has little or no influence on management outcomes for our particular group of patients. Other investigation tools such as computed tomography angiogram (CTA) and magnetic resonance angiography (MRA), although superior in terms of detecting and defining carotid and ophthalmic artery disease, are invasive and associated with a mortality risk and hence are still reserved as secondary investigations ordered by a vascular surgeon rather than an ophthalmologist.

More so, our study showed that most patients with confirmed carotid artery stenoses were managed conservatively with cardiovascular risk modulation as advised by a vascular/stroke team and no carotid surgical option was offered. We recommend that conservative treatment with aspirin and statins be commenced as soon as OIS is suspected. Most OIS patients have multiple cardiovascular co-morbidities, hence statins and low-dose aspirin may already be part of their medical treatment, thus ophthalmic specialists should reinforce this conservative treatment based on clinical ophthalmic findings with an aim to prevent OIS progression and bilateral disease.

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Disclosure

None of the authors have conflicts of interests related to this work.

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