



A Potential Pathway for Managing Diabetic Patients with Arterial Emboli Detected by Retinal Screening[☆]

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KEYWORDS

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Abstract *Objective:* The aim was to review a pathway of care for diabetic patients found to have retinal artery emboli detected by retinal screening.

Design: This was a retrospective review of a pathway agreed in 2001 by a multidisciplinary team.

Materials and methods: The prospectively collected Gloucestershire Diabetic Retinal Screening Programme database was reviewed; patients sent for carotid duplex imaging underwent review of their scan results and their casenotes.

Results: The prevalence of retinal emboli was 214 out of 25,299 diabetic patients who had retinal screening (0.85%). Some 200 diabetic patients underwent carotid duplex imaging; 23 had ipsilateral and 2 had contralateral carotid stenosis >70%. Of these, ten patients underwent carotid endarterectomy without any major morbidity.

Conclusions: A pathway was established for the small number of patients with retinal emboli, and could be tested in other populations.

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Introduction

Diabetic retinopathy is one of the commonest causes of blindness in Western populations. The aim of the English National Diabetic Retinopathy Screening Programme is to

detect retinopathy at an early stage when treatment can be offered and the rate of subsequent blindness reduced.¹

In the English programme, people with diabetes over the age of twelve are offered an annual eye test that includes a digital photograph of the retina. These images are subsequently graded for retinopathy. One of the consequences of this screening programme is that other eye disease is detected. Occasionally, asymptomatic emboli are seen on the photographs in branches of the retinal arteries. One possible cause of the emboli is atheroembolism from atherosclerotic carotid artery disease. Severe carotid disease is a risk factor for subsequent stroke.^{2,3}

With this in mind, after the first cases of embolisation were noted in the retinal screening programme in 2001,

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a multidisciplinary team that included ophthalmologists, vascular specialists and radiologists in Gloucestershire discussed the issue, and agreed that carotid disease could be the source and should therefore be excluded in diabetic patients found to have retinal arterial emboli. A pathway was created where these patients would all be offered duplex ultrasound imaging via fax referral, without vascular consultation. Any patient with severe carotid disease would be reviewed in a vascular outpatient clinic and then discussed at a vascular Multidisciplinary Team Meeting (MDT). An option for patients with carotid stenosis $>70\%$ would be carotid endarterectomy. As with other patients at the time of the study, those with ipsilateral carotid disease $<70\%$ stenosis were not, in general, offered surgery.

The present report details the outcome of patients identified through this pathway between February 2001 and October 2008. The study aimed to determine the extent of the problem within this population of diabetic patients, and whether asymptomatic retinal emboli are a useful marker for significant carotid artery stenosis.

Patients and Methods

The study population comprised those people with diabetes who were invited for screening by the Gloucestershire Diabetic Retinopathy Screening Service and were screened between February 2001 and October 2008. Electronic records were kept on attendance and the results of retinal screening in all these individuals. All patients with a retinal embolus diagnosed on digital photographic screening were referred for duplex ultrasound imaging in one of the two vascular laboratories in Gloucestershire. Reports were then sent to the vascular team who interpreted them and forwarded them to the patient's ophthalmologist and general practitioner. Patients with significant carotid disease ($>70\%$ stenosis in either carotid artery assessed using NASCET methodology)⁴ were offered an outpatient appointment with one of the vascular surgeons in Gloucestershire.

Patients with significant carotid disease were counselled about the risk of stroke. All were offered best medical therapy (antiplatelet therapy alone at the start of the study, with statins offered routinely by the end). They were counselled using a combination of the known risks of subsequent stroke for people with asymptomatic carotid stenosis,^{5,6} and those for people with symptomatic carotid disease.^{2,3} A number of patients opted to undergo carotid

endarterectomy in addition to best medical therapy in an attempt to reduce the potential risk of stroke.

The notes for all patients who had a significant carotid stenosis were reviewed and the outcome of their vascular consultation and treatment were recorded. Additional data were entered into an Excel spreadsheet, where possible data were modified to graded numeric levels to enable easier analysis using SPSS version 11.

In addition, photographs that demonstrated emboli were classified into calcium, fibrinoplatelet or cholesterol (Hollenhorst plaque) by two expert graders and a third arbitration grader (all accredited graders in the National Screening Programme) who settled any differences in opinion.⁷ These results were compared with the carotid duplex findings.

Results

Diabetic retinopathy screening service

The number of people with diabetes in Gloucestershire (population 611,011 – 2009) has risen steadily from 10,543 in 2001 to 24,918 in 2008. Diabetes affects all age groups (Fig. 1), but there is a preponderance of elderly patients who would also be at higher risk of carotid disease. The Gloucestershire Diabetic Retinopathy Screening Service commenced in 1998. All diabetic patients in Gloucestershire are offered screening to detect sight-threatening retinopathy. In 2001, 12,000 people with diabetes were offered digital retinal photography, whereas by 2008 this had risen to 24,000, a rise of over 1700 every year. The uptake rate in this population for digital photographic screening has stayed constant since it was first reported at 74%.⁸

Asymptomatic retinal artery emboli

Between 2001 and 2008 a total of 214 patients with asymptomatic retinal emboli were identified amongst 25,299 people with diabetes screened (detection rate 0.85% per diabetic; 0.11% per screen) (Fig. 2). A total of 200 of

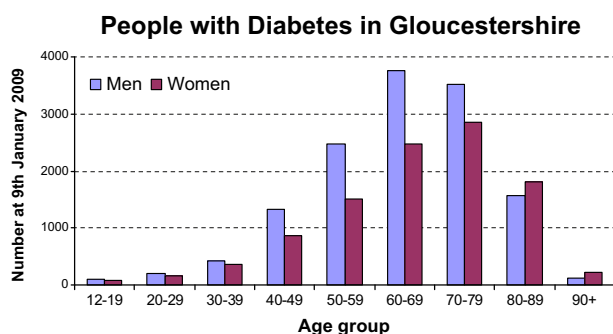


Figure 1 The age range of people with diabetes in Gloucestershire.

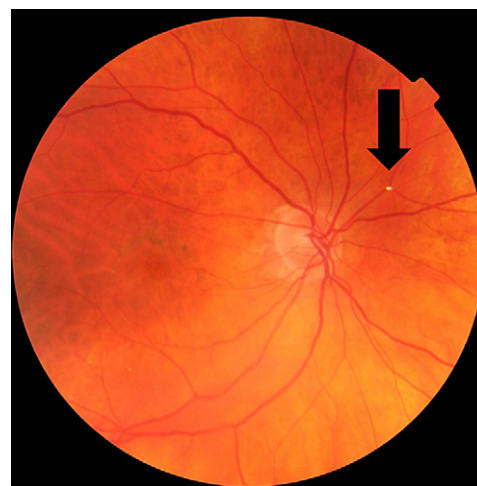


Figure 2 Digital retinal photograph showing embolus in branch retinal artery (arrow).

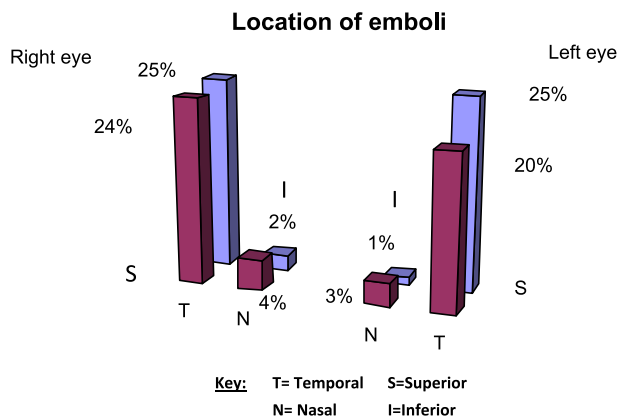


Figure 3 Location of diabetic retinal artery emboli by retinal quadrant: the majority were in the superior and temporal quadrants.

these patients had a carotid duplex scan; 14 did not for reasons that were not known. The mean age of the patients who had imaging was 72 years (median 71, range 52–93 years); 68% were men and 32% were women.

Of the 200 carotid scans, ten could not be retrieved for review. In the remaining 190, retinal-imaging graders classified the majority of emboli as cholesterol-based (78%), with calcium in 16% and fibrin in 6%. The emboli

were evenly distributed between left and right eyes; the majority were detected in the temporal arcades (Fig. 3).

The results of the 190 carotid duplex scans are shown in Table 1, both ipsilateral and contralateral to the retinal embolus. Twenty-five patients had surgically significant carotid stenosis >70%. Two patients had >70% stenosis contralateral to the retinal emboli, but the remainder were ipsilateral. All 25 were offered an outpatient appointment with a vascular surgeon and all attended. After consultation, 15 patients preferred to continue best medical therapy alone. Some declined surgery because of advanced age or serious co-morbidity (angina, dementia, critical leg ischaemia), but others simply chose to avoid surgery on the perceived balance of risks.

Ten patients opted to undergo carotid endarterectomy; all had ipsilateral carotid stenosis >70%. The mean age of these patients was 68 years (median 66, range 57–81 years). Most procedures were standard endarterectomy with Dacron patch angioplasty under local anaesthetic with sedation.⁹ All procedures were uneventful, and all patients survived. One had a postoperative hypoglossal nerve palsy that settled within six weeks.

Six of the ten were still alive at the end of the study in 2008. Of the four who died, none was known to have died from a stroke. Two died within a year of surgery (aged 67 and 71); a patient who was 66 years old at the time of surgery died after 2 years from lung cancer, and the fourth

Table 1 Results of duplex ultrasound imaging of carotid arteries ipsilateral and contralateral to the retinal artery embolus.

Degree of stenosis contralateral to embolus ↓	Degree of Stenosis ipsilateral to embolus →				Total
	Under 30%	30-69%	70-99%	Occluded	
Under 30%	64	33	6	1	104(56%)
30-69%	16	41	12	0	69(37%)
70-99%	2	2	2	0	6(3%)
Occluded	1	4	1	1	7(4%)
Total	83(45%)	80(43%)	21(11%)	2(1%)	186

patient who was 73 at the time of his surgery died five years later.

Of the 15 people with significant carotid stenosis that did not have surgery, five died during follow-up. Although detailed information about the cause of death was only available for two, none was known to have had a stroke. One of the survivors did have a stroke during follow-up, but contralateral to the retinal embolus/carotid stenosis.

The mortality rate in the whole population was generally high. Of all people with diabetes referred to the vascular service, one, three and five year mortality rates were 8, 20 and 35% respectively. Detailed information about causes of death were not available.

Discussion

This study has shown that the total number of people with diabetes who develop retinal embolism is relatively low (approximately 1%), which is actually similar to the number found in population studies of non-diabetics.¹⁰ Yet, in the UK, diabetic retinopathy screening is now a nationally funded programme, so the numbers across the country will be substantial. With the rise in obesity and poor lifestyle choices, the number of people with diabetes is likely to continue to rise exponentially. This paper has shown how a pathway can be established to process patients who have retinal emboli detected at diabetic retinopathy screening. The authors' previous pathway improved the speed at which patients accessed carotid endarterectomy via fax referral for symptomatic disease.¹¹ In fact, a relatively small number of patients with retinal emboli were found to have a significant carotid stenosis (23 ipsilateral, two contralateral). It is not clear why these were concentrated in the superior and temporal retinal fields, but as with arterial emboli elsewhere, this was presumably a result of the anatomical pathway of the arterioles supplying this area of retina. Once identified, patients with greater than 70% stenosis were counselled in outpatients. A number were not fit for intervention due to age or poor health and a greater number declined the intervention offered, and simply continued best medical therapy.^{12,13} Of the ten patients that underwent carotid intervention, all had endarterectomy mostly under local anaesthetic, without major perioperative complications. This pathway cannot be expected to make a major contribution to public health, but it is a way to manage the unexpected finding of retinal embolus.

The indications for carotid endarterectomy are becoming well understood. There is clearly a significant stroke risk after a carotid territory attack in patients with symptomatic carotid stenosis greater than 70%.^{5,6} The number needed to treat is four to five to prevent one stroke, or perhaps even fewer if the procedure is done acutely.^{14,15} The situation is also understood for people with asymptomatic carotid stenosis. Randomised clinical trials suggest that approximately 12% develop ipsilateral stroke within five years and this can be reduced by intervention to 6%.³ However, the number of carotid endarterectomies needed to treat to prevent one stroke in this group is approximately forty.

The question remains what is the risk of stroke in a patient with retinal artery emboli, (i.e., known embolisation) and

a carotid stenosis of greater than 70%? There are no natural history studies in people with diabetes, but it could be expected that the risks are at least as great as similar asymptomatic disease, and probably higher. Pooled data from studies in non diabetics suggest that these individuals have a modest increase in the risk of all cause mortality and stroke.¹⁰ The population studied here are likely to be high risk, simply from the high rate of co-morbidity. In addition, several studies have suggested that the demonstration of cerebral embolic lesions on computed tomography or magnetic resonance imaging is a risk factor for stroke.¹⁶

The agreed position after the initial MDT discussion amongst specialist colleagues was that diabetics with severe carotid stenosis and retinal emboli on screening were a high risk group, and this formed the basis for the individual discussions with patients found to have severe carotid disease. The risk of stroke after amaurosis fugax is also known to be lower than after a focal neurological event.¹⁷ It is not yet known, however, whether the asymptomatic retinal embolus will be more allied to this lower risk group. On the other hand, the advantage of a preventive procedure in this high-risk group could be questioned, since they frequently have other cardiovascular complications.¹⁸ At least an outpatient appointment can ensure that they are receiving best medical therapy.¹⁹

There are a number of significant limitations to this study. First it is not a proper epidemiological study, since the data were collected for the purposes of a screening programme, and subsequent outcome data are neither comprehensive nor secure. The surgical part of the study was retrospective, and again the late outcomes data could not be guaranteed. The small number involved means that a controlled trial is unlikely to be warranted in this group and thus observational studies such as this can supplement the judgement and recommendations of expert panels. The present paper outlines a coherent and logical approach, supported by colleagues from an eye clinic in Derbyshire.²⁰ Further research into the management of asymptomatic carotid disease and continued prospective data collection in this patient group may help identify the higher risk individuals more suitable for intervention, which may include diabetic patients with retinal emboli. The role of novel therapies such as carotid stenting will also need to be evaluated. The expanding number of diabetic patients may mean that this subject may become increasingly important as time goes by.

Conflict of Interest

The authors have no known conflicts of interest to declare.

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