Investigating retinal microvascular abnormalities and stroke with computerised image analysis

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Lay Summary

A stroke happens when the blood flow to part of the brain is interrupted. Lacunar stroke is a type of stroke which is caused by problems with the small (rather than large) blood vessels in the brain but as these vessels are so small it is difficult to image them using Magnetic Resonance (MR) or Computed Tomography (CT) brain scans. The blood vessels in the back of the eye are similar to the small blood vessels in the brain. It is easy to take a photograph of these blood vessels and to look for any abnormalities. These abnormalities or changes may mirror the changes that occur in the small vessels in the brain.

We looked for changes in the blood vessels using photographs of the back of the retina that had been processed by computer. We wrote the programmes for the software that identified the abnormalities. We found that in patients with lacunar stroke there was no difference in the small arteries (blood vessels that carry blood to the back of the eye) but that small veins (blood vessels that carry blood from the back of the eye to the heart) were wider. We also found that the branching patterns of blood vessels in patients with lacunar stroke were simpler than those in patients with other non-lacunar stroke. These findings suggest that abnormalities in the veins may be associated with lacunar stroke.

Methods

Patients presenting with lacunar stroke and with minor cortical stroke were recruited into the study. All patients were examined by a stroke expert and underwent MR brain imaging at **SBIRC** to confirm and subtype stroke. Retinal photographs of both eyes were taken in the **Edinburgh WTCRF** by digital retinal camera (see Figures 1 and 2) and with analysis supported by the **Image Analysis Core**. Novel semi-automated techniques were developed, validated and used for measuring retinal arteriolar and venular widths (see Figure 3), arteriolar bifurcation geometry (i.e. branching co-efficients which characterise cross section area across a bifurcation and branching angles) and fractal dimensions (reflecting branching complexity) of the vasculature in the image (see Figure 4).

Results

253 patients (129 lacunar stroke, 124 cortical stroke), mean age 68 years, were recruited. We found:

- retinal venules are wider in patients with lacunar strokes compared with those in patients with cortical strokes (see Table 1)[1]
- there were no difference in arteriolar widths
- there were no differences in arteriolar branching co-efficients or arteriolar branching angles between lacunar and cortical strokes, although leukoaraiosis was associated with altered branching coefficients[2]
- fractal dimensions were decreased in lacunar stroke suggesting a loss of branching complexity[3]

Discussion and Conclusions

Retinal microvascular abnormalities differ between lacunar and cortical stroke suggesting that a distinct small vessel vasculopathy may cause lacunar stroke. These results indicate that venular disease (a hitherto under-researched area) may play a role in the pathophysiology of lacunar stroke. Retinal microvascular abnormalities can act as biomarkers for cerebral small vessel disease.

Although predominantly a research tool at the moment, it is eventually hoped that retinal imaging, with further advancement, could be used to establish future disease risk for an individual in conjunction with more established tests.

References
1. Doubal FN et al *Neurology* 2009;72:1773-1778
2. Doubal FN et al *International Journal of Stroke* 2009 in press
3. Doubal FN et al *Neurology* 2010;74:1102-1107

Figure 1: Retinal camera with subject and photographer. Note the retinal image appears on the screen immediately.

Figure 2: Digital colour image of the human retina showing optic disc, arterioles and venules

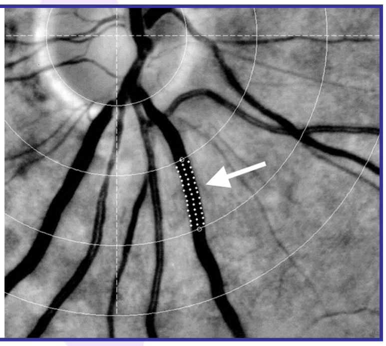

Figure 3: Grayscale image showing lower half of optic disk and surrounding arterioles and venules. Width measured by *vessel-tracking* (white arrow).

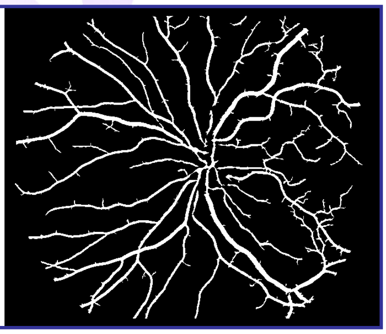

Figure 4: Retinal blood vessels automatically segmented by computer processing. This map is used to assess bifurcation geometry and vessel pattern complexity.

Table 1: Associations between vessel widths and key patient variables.

Explanatory variable	CRAE		CRVE		AVR	
	β	p Value	β	p Value	β	p Value
Age	0.03	0.12	−0.11	<0.001*	0.002	0.002
Male	−1.1	0.02*	−0.10	0.87	−0.01	0.3
Lacunar stroke subtype	-0.48	0.29	1.33	0.03*	−0.02	0.047*
Diabetes	0.02	0.97	−0.29	0.74	0.002	0.8
Hypertension	−0.95	0.05	0.94	0.15	−0.02	0.06
CRAE	NA		0.88	<0.001*	NA	
CRVE	0.48	<0.001*	NA		NA	

All analyses are corrected for the presence of the other variables in the table.
*$p < 0.05$.
CRAE = central retinal artery equivalent; CRVE = central retinal vein equivalent; AVR = arteriovenous ratio; NA = not applicable.

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