The eyes as a window to the heart: looking beyond the horizon

Ify Mordi 1, Emanuele Trucco 2

Despite significant advances in prevention and treatment, cardiovascular disease (CVD) remains a significant cause of mortality and morbidity. CVD is the most common cause of death worldwide, and its burden is increasing. 1 In the UK it accounts for a quarter of all deaths. 2 Given the morbidity associated with CVD, identification of individuals at high risk is particularly important.

Currently clinical risk scores such as the QRISK assessment tool 3 are recommended for evaluating CVD risk. 4-5 Tools such as these use a combination of clinical variables, risk factors and laboratory tests to calculate an individual’s CVD risk over a period of time (typically 10 years). If the calculated level of risk is above a set threshold then preventative therapy such as statins are recommended. These risk scores are widely validated and tend to be more accurate than clinical judgement, although some guidelines suggest that ‘risk enhancers’ such as the presence of retinopathy could be used to guide initiation of preventative therapy in certain patient groups. 6

Perhaps one of the main reasons for this lack of clinical translation is that the expertise required to assess the retina, particularly quantitatively, is limited, and the process itself is of course time-consuming. Software tools have been developed to semi-automate the analysis of the retinal vasculature, 7-17 and morphometric measures such as vessel tortuosity, diameter and fractal dimension have been associated with increased CVD risk in multiple studies. 18-20

Taking this a step further, in this issue, the paper by Rudnicka et al 21 describes the use of a fully automated artificial intelligence (AI)-enabled retinal assessment tool for prediction of CVD risk in two large population cohorts. The software tool, QUARTZ, computes estimates of vessel width, area and tortuosity efficiently. Over 70,000 individuals were included, the majority of whom did not have any prior history of CVD. The authors found that the retinal measurements computed by QUARTZ were significantly associated with CVD (death, myocardial infarction and stroke), with similar predictive performance to the Framingham clinical risk score. The results strengthen the evidence from several similar studies that the retina can be a useful and potentially disruptive source of information for CVD risk in personalised medicine. As the authors discuss, the accessibility of large repositories of retinal photography does make this concept particularly attractive as it enables validation of hypotheses in large, richly phenotyped cohorts.

So, what next? Beyond demonstrating the association between retinal vascular features and CVD, we must consider how this knowledge could be integrated into clinical care. A number of questions remain.

1. Who would conduct such a retinal screening programme? Using retinal screening in this way would presumably require a significant increase in the number of ophthalmologists or otherwise trained assessors. Introducing AI would perhaps lessen this burden, although some clinicians may have concerns about the ‘black box’ aspect of machine learning and AI technology. 22-24

2. Who would act on any CVD risk findings? Would ophthalmologists be expected to prescribe preventative CVD therapies, or would cardiologists and primary care practitioners be supported in taking on this additional workload? As with many aspects of modern clinical care, a multidisciplinary team approach is likely to be optimal. This requires of course a very significant coordination and regulatory effort at national level.

3. How should the data be translated to clinical practice? Despite increasing evidence showing that retinal vascular findings can predict CVD risk, the implications of introducing such a screening programme in the general population mean that a higher standard of evidence—that is, a large, randomised clinical trial—is surely required before the CVD risk prevention guidelines can be changed to incorporate retinal measurements as part of our routine risk prediction assessment. While a one-off retinal measure may be associated with adverse CVD outcome, is this risk modifiable? Observational findings that seemed plausible but did not translate to positive clinical intervention targets abound in the scientific literature. It also seems unlikely that retinal assessment alone could be used as a risk predictor, but it could indeed form part of a comprehensive CVD risk assessment incorporating other clinical risk factors. Even using AI, in this study by Rudnicka et al 21 around 20% of the images were not of sufficient quality to be assessed using QUARTZ.

Looking to the future, there have been numerous studies reporting consistent associations between retinal vascular parameters and CVD prognosis. The retina may indeed provide a rich source of prognostic information relating to CVD risk. What is now needed is for ophthalmologists, cardiologists, primary care physicians and computer scientists to work together to design studies to determine whether using this information improves clinical outcome, and, if so, to work with regulatory bodies, scientific societies and

1 Division of Molecular and Clinical Medicine, School of Medicine, University of Dundee, Dundee, UK
2 VAMPIRE project, Computing, School of Science and Engineering, University of Dundee, Dundee, UK
Correspondence to Dr Ify Mordi, University of Dundee, Dundee, UK; i.mordi@dundee.ac.uk

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healthcare systems to optimise clinical workflows and enable practical implementation in routine practice.

Twitter Ify Mordi @docifymordi
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ORCID ID
Ify Mordi http://orcid.org/0000-0002-2686-729X

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