Utility of Ward-Based Retinal Photography in Stroke Patients

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Background: Improvements in acute care of stroke patients have decreased mortality, but survivors are still at increased risk of future vascular events and mitigation of this risk requires thorough assessment of the underlying factors leading to the stroke.The brain and eye share a common embryological origin and numerous similarities exist between the small vessels of the retina and brain. Recent population-based studies have demonstrated a close link between retinal vascular changes and stroke, suggesting that retinal photography could have utility in assessing underlying stroke risk factors and prognosis after stroke. Modern imaging equipment can facilitate precise measurement and monitoring of vascular features. However, use of this equipment is a challenge in the stroke ward setting as patients are frequently unable to maintain the required seated position, and pupil dilatation is often not feasible as it could potentially obscure important neurological signs of stroke progression. *Materials and Methods:* This small study investigated the utility of a novel handheld, nonmydriatic retinal camera in the stroke ward and explored associations between retinal vascular features and stroke risk factors. This camera circumvented the practical limitations of conducting retinal photography in the stroke ward setting. *Results:* A positive correlation was found between carotid disease and both mean width of arterioles ($r = .40$, $P = .00571$) and venules ($r = .30$, $P = .0381$). *Conclusions:* The results provide further evidence that retinal vascular features are clinically informative about underlying stroke risk factors and demonstrate the utility of handheld retinal photography in the stroke ward. **Key Words:** Stroke—retina—vascular—aging—risk factors.

Introduction

Stroke is one of the leading causes of mortality and disability worldwide.[1] In Australia, stroke is the third single greatest killer after coronary heart disease and dementia, and a leading cause of disability.[2] It is estimated that in the next 10 years more than half a million Australians will suffer a stroke and of these, 1 in 5 will die within a month, and 1 in 3 die within a year.[3] The total financial cost per year in Australia due to stroke was estimated to be $5 billion in 2012.[4]

Improvements in acute care of stroke patients have decreased mortality, but survivors have an increased risk of subsequent stroke of 43% over 10 years, with an annual rate of about 4%.[5] Additionally, there is convincing evidence that poststroke interventions such as antithrombotic therapy, carotid revascularization, and control of causal risk factors are efficacious in reducing the risk of recurrent stroke.[5] Hence, evaluating the underlying factors leading to stroke is critical to improving prognosis.

Small vessel disease has been implicated in the development of stroke,[6] but the cerebral small vessels remain

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difficult to assess clinically. The retina, however, can be imaged easily, repeatedly, and noninvasively through the transparent layers of the eye. The retina is a developmental outgrowth of the brain and shares anatomical and regulatory similarities in both micro- and macrovasculatures.[7-13] The essentially 2-dimensional nature of the retinal vasculature also means it can be easily analyzed. The retina uniquely allows direct, noninvasive investigation of both microvasculature and central nervous system tissue, providing a valuable window into both systemic vascular and cerebral health[14]; hence, noninvasive retinal imaging is being researched as a method for detecting pathology potentially affecting the brain.

Microvascular changes in the retina have been found following stroke,[15-17] and particular retinal vascular changes may be useful as prognostic markers following stroke and also may improve the understanding of novel vascular risk factors and stroke pathophysiology.[18]

Although community screening for retinal small vessel disease may one day have utility in assessing stroke risk, assessing underlying causes and prognosis for poststroke patients poses additional challenges. Traditional retinal imaging techniques involve dilatation of pupils and require that the patient is mobile enough to submit to formal retinal photography, sitting in front of a large, table-mounted camera. Direct retinal viewing with a handheld ophthalmoscope also requires dilatation of pupils and is less accurate and highly user dependent. Pupil dilatation is often not feasible in an acute stroke setting as it could potentially obscure important neurological signs of stroke progression, and it is often not possible for stroke patients to be moved to and seated in front of a table-mounted camera for retinal imaging.

With the progression of technology we now have access to handheld retinal cameras with nonmydriatic (without pupil dilatation) capabilities. These cameras can be used while patients are lying down and have the potential to allow practical assessment of the retinal small vessels in the acute poststroke setting.

This observational cohort study investigated the feasibility and usefulness of ward-based, handheld, nonmydriatic retinal photography as a tool to screen for retinal signs of disease that may improve diagnosis of the etiology of acute ischemic and hemorrhagic strokes, facilitate relevant investigations and appropriate preventive treatments, and improve the prediction of risk of recurrent stroke and other major vascular events. A nonmydriatic, handheld retinal camera (Merge EyeScan, Merge Healthcare, Chicago, IL) was trialed in a stroke ward-based setting. The feasibility of this approach was evaluated and retinal photos were used to screen for retinal signs of disease processes known to be risk factors in acute stroke, including both clinician grading and automated computer-based grading of retinal images.

Automated computer-based grading was utilized to investigate retinal vessel width and fractal dimension of the vessel network, previously reported to be associated with risk of incident stroke[19-21] and hemoglobin level,[22] respectively. Retinal emboli and many signs of hypertensive and diabetic retinopathies have been reported to be associated with prevalent stroke, incident stroke, and stroke mortality, independent of blood pressure and other cerebrovascular risk factors.[17,23-25] Hence, in the present study, retinal images were graded by a clinician for emboli and signs of retinopathy (microaneurisms, hemorrhages, cotton wool spots, arteriovenular nicking, hard exudates, tortuosity, venous beading, neovascularization, and intraretinal microvascular abnormality [IrMA]).

This study investigated whether nonmydriatic retinal photography could be a useful, ward-based tool in the setting of acute stroke for detecting disease processes known to be risk factors in stroke.

Materials and Methods

Study Population

Patients were recruited from the stroke ward of the Royal Perth Hospital (RPH), Perth, Australia. Patients 18 years of age or older presenting to the acute stroke unit at RPH within 7 days of onset were recruited from December 2012 to January 2014. Patients who lacked the cognitive or physical ability to submit to ward-based nonmydriatic retinal photography were excluded, as were those who lacked the cognitive ability to provide informed consent and whose next of kin identified reasons why they would not be suitable for a waiver of consent. Prior to the study, approval was obtained from the RPH ethics committee, and all participants gave written informed consent.

Retinal Photography

Retinal photography took place at the patient's bedside using the Merge EyeScan camera, a handheld, portable nonmydriatic digital retinal camera. The camera has a field of view of 45° and a 5.3-megapixel sensor and has been used in previous clinical studies of the retina.[26-28] Digital retinal color photographs (disk centered and macula centered) were collected from both eyes without pupil dilatation. Retinal photography was conducted in the RPH stroke ward.

Interpretation was performed by a combination of grading using semiautomated image processing and qualitative grading by a clinician. Graders were supervised by clinical retinal specialist ophthalmologists in both cases, in line with methods used in previous studies.[15,18,29] Blinding of clinical details occurred for both the automated analysis and human grading.

Clinician Assessment of Retinal Photographs

Color retinal photographs were examined by an experienced ophthalmologist for the following signs: emboli, microaneurisms, hemorrhages, cotton wool spots, arteriovenular nicking, hard exudates, tortuosity, venous beading, neovascularization, and IrMA. Only images