Detection of new neovascular AMD in at-risk eyes using a handheld radial shape discrimination test in a clinical population

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Introduction

The advent of effective treatments for neovascular age-related macular degeneration (nAMD) has transformed the visual prognosis for patients. As early detection and treatment lead to improved visual outcomes, there is a need for improved means of detection and monitoring. Wang et al (2013) demonstrated that the ability of patients to detect systematic deformations in radial frequency patterns was related to the severity of macular disease.

Aim: To investigate the performance of the handheld Radial Shape Discrimination (hRSD) test in detecting the development of nAMD in the disease-free fellow eyes of patients being treated for nAMD in their first eye.

Methods

The hRSD test

We used the S4MC version of the hRSD test. Stimuli, presented on an Apple iPod Touch, were three radial frequency patterns (2.5 cycle/diameter), one of which (the target to be detected) was sinusoidally modulated (frequency = 8 cycles, Fig 1). Modulation amplitude was controlled by a staircase procedure, to establish the threshold for detecting distortion. The result was expressed as a logMAR value.

Participants

Participants, recruited from a local AMD clinical service, were tested during up to 12 routine clinical visits, 1-2 months apart. The study eye was the non-affected eye of participants with unilateral nAMD (for which they were being treated and monitored) and was confirmed to have no nAMD or central geographic atrophy (CGA), with a VA of 0.4-logMAR or better.

Procedures

At each visit the hRSD test was performed monocularly on the undilated study eye, and all possible checks, including the treated eye, with optical correction for viewing at 40cm. Other clinical information was obtained from patients’ clinical notes. Diagnosis of the development of nAMD was based upon slit-lamp examination and Spectral OCT scans, and confirmed by fluorescein angiography in all cases. Examining clinicians were blinded to the hRSD results. Treatment was initiated in all patients who converted to nAMD in the study eye.

Analysis

Demographic information, hRSD results and other information (eg BCVA) were collated in an MS Excel spreadsheet, and statistical analysis conducted using SPSS. For all participants who converted to nAMD, further checks of OCT scans were conducted to rule out undocumented central GA. Study eyes that developed nAMD during follow-up were classed as “converters”, those that did not were classed as “controls”.

Results

Of 124 participants recruited (mean±SD age: 78±7y; range 58-92y; 38 male, 86 female), 17 (14%) were diagnosed with nAMD in the study eye during follow-up. Converters were predominantly female (15/17) and slightly older than Controls (81±7y vs 77±5y).

In Converters, the change in hRSD threshold and change in VA from baseline to conversion in the study eye was from -0.50±0.19 to -0.43±0.16 logMAR and from 0.07±0.14 to 0.17±0.18logMAR respectively (Figure 3; nAMD mean difference: 0.08±0.19 logMAR units; paired t-test: t=1.7, df=15; p=0.12; VA mean difference: 0.09±0.18logMAR; t=0.34; df=73).

A comparison of the distribution of hRSD scores for four types of eyes in Figure 4 illustrates the difficulty of detecting recent-onset nAMD in at-risk eyes. ROC analysis showed that for the clinically relevant discrimination (between at-risk eyes and new nAMD) test performance was moderate (AUC=0.75; Figure 5a). When data from healthy eyes and eyes with established disease (treated eyes) is included, test performance improved (AUC=0.92; Figure 5a). While there was a relationship between hRSD scores and BCVA (Figure 4a), central subfield thickness (CST) was not related to hRSD scores (Figure 4b). However, there was a statistically significant difference between CST in converters (at conversion: 332±56μm) and controls (278±25μm; t=4.7; df=12; p<0.001).

ROC analysis of the critical data (Figure 5a) demonstrated moderate test performance. Previously Wang et al (2013) reported in a smaller group of patients that at a cut-off hRSD score of 0.37logMAR, sensitivity and specificity for distinguishing intermediate and exudative AMD was 89% and 79% respectively. In our larger prospective study, performance was poorer although comparable to TD-OCT and PPPK; and better than Amsler grid when these tests were in a similar study design (Table 1).

Discussion

Detecting nAMD promptly faces the challenge illustrated in Figure 4. While test performance is often assessed by comparing healthy eyes to eyes with established disease (i.e. seeking to distinguish between distributions vs AUC), the clinical challenge is to distinguish between at-risk eyes and the development of early neovascularisation (i.e. distinguishing between and among these groups.)

At recruitment participants who would eventually develop nAMD had similar hRSD scores and VA to non-converters (Figure 2), at conversion their hRSD performance was poorer, even though VA remained relatively stable (Figure 3).

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Conclusions

In the critical diagnostic context, hRSD test performance is moderate.

It performs as well, or better than, alternative tests when these are in an intermediate stage in similar patients.

Given the ease of use of this handheld visual function test, and its inexpensiveness, its role in screening should be further investigated.

References


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