Diabetic Neuropathy: Retinal Biomarkers of Peripheral Disease

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ISDR

Introduction

- Diabetic Peripheral Neuropathy (DPN) is one of the common microvascular complications of diabetes (Juster-Switlyk and Smith, 2016)
- There is currently no consensus on the best method to test DPN
- OCT is a non-invasive imaging technique that allows visualisation and measurement of individual retinal layers
- NFL/GCL thinning has been associated with DPN
- The ISDR cohort study has collected data on people with diabetes in Liverpool: primary care systemic variables and complications screening; Diabetic Retinopathy (DR) screening episodes; Hospital Eye Service (HES) appointments
- Patients referred to the HES from the DR screening programme undergo macular OCT imaging
- We hypothesise that NFL and GCL is decreased in patients with DPN that are referred to HES from community DR screening

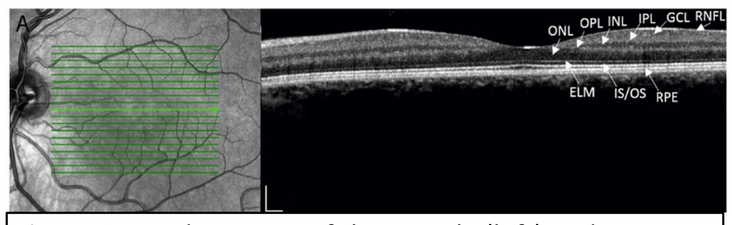

Figure 1- Fundus image of the macula (left) and cross-sectional retinal image (right) using OCT imaging (Self et al, 2017).

Objectives

1. To calculate the prevalence of DPN in ISDR study participants referred to the HES from DR screening
2. To investigate the associations of DPN with markers of retinal neuropathy and systemic variables

Methods

- Retrospective, observational cross-sectional study
- Participants with documented DPN results and suitable OCT images in their first HES appointment between 2012-2017 were selected for analysis
- DPN was defined as present/absent on the basis of the 10 g monofilament test in primary care
- Systemic variables (including demographics, HbA1c and Blood pressure) were tested in primary care
- DR grading and macular OCT images from HES appointments was documented
- Automated segmentation and calculation of NFL and GCL thickness was done using a fully convolutional neural network
- Univariate analyses and multiple logistic regression were performed to investigate associations between retinal biomarkers, systemic variables and DPN

Results

Patient characteristics

- 269 patients (47.7%) were included for analysis from the initial 564 patients that were screened for inclusion
- 52.3% of patients were male, the median age of the cohort was 48.5 years old (IQR 22) and the predominant ethnicity was white (83.9% White, 6.7% Asian, 6.3% Black, 0.4% Chinese and 2.7% Mixed ethnicity)

Prevalence of DPN

- The prevalence of DPN in this population was 12.3% (95% CI: 8.3%, 16.2%). DPN was present in 33 patients and absent in 236 patients

Relationships between variables (Figure 3, Table 1)

- Biomarkers of retinal neuropathy were not significantly different between DPN groups
- Age (mean 6.9 years (p=0.03; OR 1.03) and male sex proportion (72.73% DPN present v 52.54% absent (p=0.03; OR 2.41)) was significantly higher in patients with DPN. There were no other significant differences between DPN groups
- Multivariate analysis of mean NFL thickness, HbA1C and age between DPN groups revealed significantly higher HbA1c (p=0.02; OR 1.02) and age (p=0.01; OR 1.043) in patients with DPN

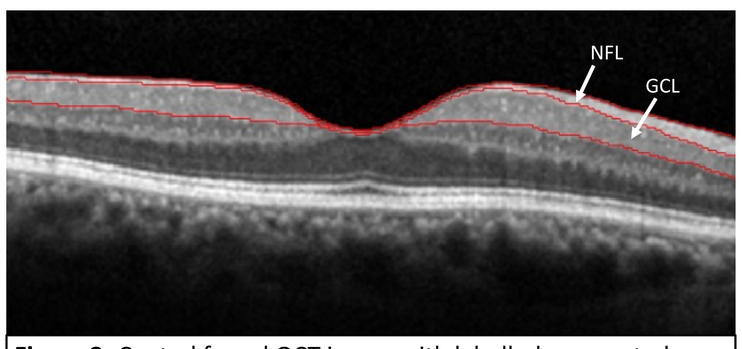

Figure 2- Central foveal OCT image with labelled segmented retinal layers.

Figures

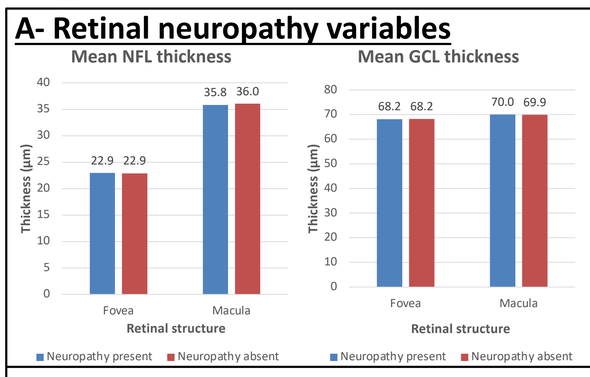

Figure 3 (A-D)- Graphs to show raw differences in variables in DPN present and absent patients.

Table 1- Odds ratios of clinical variable differences between patients with and without DPN through univariate and multiple logistic regression analysis.

Univariate analysis				
Clinical Variable	Odds ratio	95% Confidence interval		Significance value (P<0.05)
		Lower limit	Upper limit	
Retinal neuropathy variables				
NFL Fovea	1.006	0.902	1.122	0.919
NFL macula	0.990	0.917	1.068	0.790
GCL fovea	1.000	0.949	1.052	0.989
GCL macula	1.002	0.945	1.063	0.938
Demographic variables				
Age	**1.028**	**1.003**	**1.053**	**0.026**
Sex	**2.409**	**1.074**	**5.401**	**0.033**
Systemic variables				
Duration of diabetes	0.982	0.928	1.040	0.544
Systolic blood pressure	0.995	0.969	1.021	0.695
HbA1c	1.009	0.992	1.025	0.305
Albumin-creatinine ratio	1.006	0.995	1.016	0.280
Total cholesterol	1.186	0.791	1.780	0.410
Multivariate analysis				
Mean NFL macular thickness	0.994	0.915	1.079	0.878
Age	**1.043**	**1.012**	**1.075**	**0.006**
HbA1c	**1.022**	**1.003**	**1.041**	**0.024**

Conclusions

- Prevalence of DPN in this population was 12.3%
- No significant differences between retinal neuropathy markers in DPN present and absent groups were found.
- Significant associations were found with increasing age and male sex in patients with DPN.
- HbA1c was also significantly associated with DPN in the multivariate analysis.

Discussion

- The results suggest that these retinal neuropathy biomarkers may not good be good predictors of DPN
- This is in contrast to literature, finding associations of retinal OCT measurements (Shahidi et al., 2012)(Salvi et al., 2016)
- Alternative reason for the results may be inaccuracy of 10 g monofilament test for DPN
- This expressed the need for new, more sensitive and specific test for DPN

References

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