**Abstract for ARVO Meeting 2016**

**Title: Endothelial dysfunction in people with diabetes in Sub-Saharan Africa: relationships with retinopathy progression and mortality**

Philip Burgess1, Theresa J Allain2, Gerald Msukwa3, Petros C Kayange2,3, Frank Mbewe4, Marta Garcia-Finana5, Simon P Harding6

1. Malawi-Liverpool-Wellcome Clinical Research Programme, Blantyre, Malawi

2. College of Medicine, University of Malawi

3. Lions First Sight Eye Hospital, Blantyre, Malawi

4. Lions First Sight Eye Hospital, Zomba, Malawi

5. Department of Biostatistics, University of Liverpool, UK

6. Department of Eye and Vision Science, University of Liverpool, UK

**Purpose:** Sub-Saharan Africa faces an epidemic of diabetes. Both diabetes and its complications are associated with endothelial dysfunction. We performed a case-control study nested within a larger prospective cohort study of diabetic retinopathy in Southern Malawi. We report serum levels of endothelial biomarkers and *in vivo* endothelial function and relationships with progression of retinopathy and mortality.

**Methods**: Subjects for the main cohort study were systematically sampled from two hospital-based diabetes clinics. Endothelial function was studied in a subset of subjects in 4 groups: (1) subjects with diabetes and sight threatening diabetic retinopathy (STDR) at baseline, (2) subjects with diabetes and diabetic retinopathy but without STDR, (3) subjects with diabetes but without retinopathy, (4) subjects without diabetes (recruited from spouses of patients attending the diabetes clinics). Clinical examination and biochemical testing was performed to assess visual acuity, glycaemic control, systolic BP, HIV status, and plasma levels of VEGF, sVCAM-1, sICAM-1, E-selectin and CRP. *In vivo* testing of endothelial function was performed using digital pulse amplitude tonometry. Retinopathy was graded with modified Wisconsin grading using 4-field mydriatic photography: dual grading with arbitration at an accredited reading centre.

**Results:** Endothelial function at baseline was studied in 179 subjects. E-selectin level correlated with HbA1c (r=0.713, p=0.001) and was higher in subjects with HIV (unpaired t-test, p=0.015). A fitted multiple linear regression model showed a significant difference in mean serum VEGF between subjects with and without diabetes but not between subjects with and without diabetic retinopathy or between subjects with and without STDR. Serum level of VEGF and E-selectin was significantly, positively associated with presence of diabetes in multiple logistic regression. Endothelial function was also investigated in relation to progression of retinopathy and mortality at 24 months. Two (or more) step progression on the Liverpool Diabetic Eye Study scale was observed in 24 subjects (19.2%; 12.3-26.1 95% CI). Neither VEGF, ICAM-1, E-selectin, VCAM-1, CRP or peripheral artery tonometry index at baseline were associated with progression of retinopathy based on univariate or multivariate regression analyses. Serum VCAM-1 was associated with death in multivariate regression.

**Conclusions:** This study provides the first evidence from sub-Saharan Africa of endothelial dysfunction in subjects with diabetes and of an association between levels of endothelial biomarkers and mortality in these subjects. No difference was observed in markers of endothelial dysfunction between subjects in whom retinopathy progressed and those in whom it did not.

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