Results: After RH mitochondrial metabolism is altered as baseline, OCR was increased, but OCR-associated adenosine triphosphate (ATP) production, coupling efficiency and spare respiratory capacity were decreased, in conjunction with an increase to proton leak and non-mitochondrial OCR. After RH, HPAs had an increased dependency on fatty acids, which may contribute to elevated baseline OCR. Following RH, HPA glycolytic metabolism was also enhanced; baseline ECAR was increased, and upon reperfusion of glucose following aglycaemia, ECAR was also augmented. We also detected increased pentose phosphate pathway activity following RH.

Conclusions: Astrocytic OCR, fatty acid oxidation, ECAR and pentose phosphate pathway activity are enhanced by RH, indicating potential adaptations to better maintain energy supply during future metabolic stress such as hypoglycaemia.

Microvascular

A65 (P462)
Retinal microvascular biomarkers are associated with incidence and progression of diabetic retinopathy in Type 2 diabetes: A GoDARTS-VAMPIRE study
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Aim: Early risk prediction of diabetic retinopathy (DR) would significantly enhance clinical prevention strategies. We aimed to determine the value of retinal vascular parameters (RVPs) as biomarkers for incidence and progression of DR from 4,461 patients with Type 2 diabetes.

Method: We used VAMPIRE 3.1 software to measure central retinal artery and vein equivalent, their ratio (artery and vein ratio, AVR), arteriodil and venular tortuosity (Torta, TortV), and fractal dimension (Da, Dv) in diabetes retinal screening photographs (DRS) in GoDARTS. Cox’s proportional hazards were used to model the impact of RVPs on DR incidence and progression, adjusted for mean HbA1c, mean systolic blood pressure (SBP) and age at diabetes diagnosis.

Results: From a total of 3,452 patients with no DR at DRS date, there were 107 incident cases during a mean follow-up of 5.8 years. Higher central retinal venular equivalent and TortV increased risk of incident DR, independently of HbA1c and SBP. Combining these two RVPs as a score, the hazard ratio was 4.2 (95% confidence interval, CI, 2.1 to 8.5) comparing the highest and lowest tertiles. From a total of 3,082 patients with mild to moderate DR at DRS date, there were 293 cases of DR progression to a higher grading. Lower AVR and Da and higher TortV were independent predictors. Combining these as a score, the hazard ratio was 1.7 (95% CI 1.4 to 2.7) comparing the highest and lowest tertiles.

Conclusions: RVPs are strong independent predictors of DR incidence and progression. Automated image processing tools such as VAMPIRE could be utilised in screening programmes to optimise targeted prevention.

A66 (P517)
Disease burden in young adults with Type 2 diabetes: A retrospective study
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Aim: To review the treatment regimens and complications in young adults (age less than 40 years) with Type 2 diabetes.

Method: A retrospective study of young adults with Type 2 diabetes. Data collected retrospectively through electronic database of Young Adult Type 2 Diabetes Clinic.

Results: Twenty-five young adults with Type 2 diabetes were included in the study. Out of 25 patients in total, male and female participants were 12 and 13, respectively. A mean age at diagnosis of Type 2 diabetes was 22 years. The mean body mass index at diagnosis was 34.4 and at review point was 33.4. The mean HbA1c at diagnosis was 82mmol/mol (SD ± 37.56) and at review point was 70.7mmol/mol (SD ± 34.62). Sixteen per cent of the patients at review point were on metformin alone, 36% on metformin with other oral agents, 28% on metformin with Glucagon-like peptide-1 receptor agonists and 20% on insulin along with oral agents. Forty-eight per cent of the patients developed diabetes-associated complications that includes fatty liver disease present in 16%, microvascular complications (proteinuria and retinopathy) present in 12% and macrovascular complications (coronary artery disease, hypertension and dyslipidaemia) present in 20% in a mean period of five years.

Conclusion: Forty-eight per cent of the patients developed diabetes-associated complications in a mean period of five years. More research and guidelines in the management of this challenging group is needed as long-term effects of the new therapies are not known and side-effect burden may contribute to poor compliance with treatment.
**A67 (P321)**

**Association between retinal vascular traits and retinopathy and renal disease in people with Type 2 diabetes: A cross-sectional analysis of the Edinburgh Type 2 Diabetes Study**

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**Aims:** Recently developed retinal vessel analysis tools offer a unique platform to evaluate the retinal microvasculature as an analogue for systemic vascular disease. The aim of this study is to determine if there is an association between retinal vessel traits and retinopathy or renal disease in a cross-sectional analysis of the Edinburgh Type 2 Diabetes Study.

**Methods:** A cohort of 1,066 adults aged 60 to 75 years with Type 2 diabetes was evaluated. Retinal images were analysed using VAMPIRE software for central retinal arteriolar equivalent, central retinal venular equivalent (CRVE), arteriolar and venular tortuosity and fractal dimension. Renal disease was defined as low glomerular filtration rate (<60ml/min/1.73 m²) or increased albumin-to-creatinine ratio (>2.5mg/mmol in men and >3.5mg/mmol in women).

**Results:** A total of 339 (31.8%) participants had diabetic retinopathy and 323 (30.3) had renal disease. After adjusting the model for various covariates, we found evidence of an association between CRVE and retinopathy (odds ratio, OR, 1.05; 95% confidence interval, CI, 1.02 to 1.08; p = 0.001) and arterial tortuosity and retinopathy (OR 1.15; 95% CI, 1.01 to 1.31; p = 0.032). Similar associations were not found between retinal traits and renal disease.

**Conclusions:** Increased CRVE and arteriolar tortuosity were found to be associated with retinopathy. Further longitudinal data and analysis, as well as exploration of retinal vascular traits, is needed to analyse these associations for and utility as a biomarker to help determine those most at risk for vascular complications of Type 2 diabetes.

**A69 (P245)**

**Corneal endothelial damage is related to corneal nerve fibre loss in patients with diabetes**

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**Aim:** The purpose of this study was to assess corneal endothelial cell morphology in relation to corneal nerve fibre damage using confocal microscopy (CCM).

**Methods:** We have studied 41 subjects with diabetes (age 54.2 ± 2.3, The International Federation of Clinical Chemistry (IFCC) 56.3 ± 3.6, duration of diabetes 12 ± 2 years) and 28 age-matched controls (age 49.2 ± 2.65) using CCM. Corneal endothelial cell density (cell/µm²), area (µm²), polymegathism (coefficient of variation) and pleomorphism (hexagonality coefficient) and corneal nerve fibre density (no/µm²), length (mm/µm²) and branch density (no/µm²) were assessed in images obtained from the central cornea.

**Results:** Corneal endothelial cell density (3,338.59 ± 43.04 vs 3,306.41 ± 39.10, p = 0.01) was reduced, and endothelial cell area (243.77 ± 3.34 vs 230.30 ± 2.77, p = 0.01) and perimeter (55.78 ± 0.41 vs 54.36 ± 0.32, p = 0.02) were increased in patients with diabetes compared with controls. There were no significant differences in cell polymegathism and pleomorphism between patients and controls. Corneal nerve fibre density (24.92 ± 0.98 vs 36.1 ± 1.42, p < 0.0001), branch density (58.1 ± 4.73 vs 91.4 ± 7.31, p < 0.0001) and length (23.16 ± 1.01 vs 26.02 ± 1.08, p = 0.03) were reduced in patients with diabetes compared with controls. Endothelial cell density was associated with corneal nerve fibre density (CNFD) (r = 0.3, p = 0.01) and corneal nerve fibre length (CNFL) (r = 0.3, p = 0.01). CNFD was significantly associated with endothelial cell density (r = 0.3, p = 0.01), area (r = −0.3, p = 0.01) and perimeter (r = −0.2, p = 0.04). CNFL was significantly associated with density (r = 0.3, p = 0.01), area (r = −0.3, p = 0.01) and perimeter (r = −0.3, p = 0.02). Endothelial cell density (3,275.75 ± 67.24 vs 3,386.76 ± 57.5, p = 0.01) was reduced, and area (248.98 ± 5.69 vs 239.86 ± 4.38, p = 0.01) and perimeter (56.3 ± 0.68 vs 55.37 ± 0.53, p = 0.02) were increased in patients compared with controls.

**A68 (P392)**

**Cardiac autonomic neuropathy predicts rapid progression of renal dysfunction in patients with diabetes-related foot disease**

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**Background:** Patients with diabetes-related foot disease are at high risk of renal dysfunction. Cardiac autonomic neuropathy (CAN) is a risk factor for renal function decline. It is unknown if CAN predicts significant renal function decline in patients with diabetic foot disease.

**Aim:** We investigated in a prospective observational study if CAN predicts progression of renal dysfunction [determined by estimated glomerular filtration rate (eGFR)] in patients with diabetic foot disease.

**Methods:** We studied 101 consecutive patients with Type 1 (n = 28) and Type 2 (n = 73) diabetes attending a tertiary centre multidisciplinary foot clinic. CAN was diagnosed by cardiac autonomic reflex tests. Median (range) follow-up was 22 (9 to 35) months. Patients were categorised in to those with (eGFR fall >5ml/min/year) or without (<5ml/min/year) rapid progression of renal dysfunction.

**Results:** Of the 101 patients, 38% had CAN at baseline. There were no significant differences in clinical and biochemical parameters between patients with and without CAN. Patients with CAN had a faster rate of eGFR decline vs those without CAN [mean 95% confidence interval (CI), −6.5 (−9.6 to −3.9) ml/min/year vs −1.87 (95% CI −4.05 to 0.63) ml/min/year, p = 0.02]. Nearly, 38% of the cohort had rapid progression (eGFR fall >5ml/min/year). In multivariate analyses, presence of CAN was a significant predictor of rapid progression [odds ratio 2.6 (95% CI 1.003 to 6.98), p < 0.05], independently of traditional cardio-renal risk factors.

**Conclusion:** Patients with diabetic foot disease and CAN have a faster rate of renal function decline. Presence of CAN identifies these high-risk patients and is an independent risk factor for renal dysfunction in this cohort.
Conclusion: This study shows corneal endothelial cell abnormalities and corneal nerve damage in patients with diabetes and they are associated with each other.

A70 (P402)
Younger age, Afro-Caribbean ethnicity and residual albuminuria predict progression of renal dysfunction: A 10-year follow-up study of patients with diabetic kidney disease on renin-angiotensin system blockade
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Background: There is a need to identify clinical parameters that predict significant progression of diabetic kidney disease (DKD).

Aims: We studied 266 (19% Type 1 diabetes) patients with DKD all on renin-angiotensin system (RAS) blockade with baseline estimated glomerular filtration rate (eGFR) >45 ml/min/1.73 m² over a median 10-year follow-up to identify variables that predict significant renal function decline defined as eGFR fall >5 ml/min/1.73 m²/year. In a cause-specific Cox proportional hazards model, predictors of end-stage renal disease (ESRD dialysis or transplantation) were also evaluated.

Results: Mean ± SD, age was 58.7 ± 12 years, systolic blood pressure 140 ± 21 mm Hg, and diastolic blood pressure 80 ± 11 mm Hg. Median (interquartile range) baseline eGFR was 69 (57 to 87) ml/min, duration of diabetes 12 (7 to 19) years, urine albumin-to-creatinine ratio (ACR) 12.2 (2 to 30) mg/mmol. Median (range) follow-up was 10 (2 to 12) years. Of the cohort, 25% of Type 1 diabetes and 23% Type 2 diabetes had an eGFR fall >5 ml/min/year. In Type 1 diabetes (n = 50), diabetes duration [odds ratio (OR) and 95% confidence interval (CI), OR 0.74 (0.56 to 0.99)], baseline eGFR [1.09 (1.01 to 1.17)] and ACR [9.5 (1.35 to 66.7)] were independent predictors of eGFR fall >5 ml/min/year (p < 0.05 for all). Similarly for Type 2 diabetes cohort (n = 216, 40% Afro-Caribbean), baseline eGFR [OR 1.04 (1.02 to 1.06)] and ACR [OR 1.4 (1.05 to 1.86)] were independent predictors (p < 0.05 for both). In the Type 2 diabetes, cohort 20% (n = 44) developed ESRD. ESRD was independently predicted by younger age, Afro-Caribbean ethnicity and ACR.

Conclusions: In patients with DKD, residual albuminuria despite RAS blockade is an independent predictor of significant renal function decline and ESRD. Younger age and ethnicity increase risk of ESRD in Type 2 diabetes.

Nick Hales Young Investigator Award

A71 (P115)
Association of tryptic peptides with progression of kidney disease in Type 1 diabetes
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Aims: To identify biomarkers associated with and predictors of renal function decline in patients with contemporary Type 1 diabetes.

Methods: From the Scottish Diabetes Research Network Type 1 Bioresource (SDRNT1BIO) cohort of 6,127 people representative of the adult population with Type 1 diabetes in Scotland, we selected 789 patients with estimated glomerular filtration rate (eGFR) >70 ml/min/1.73 m² at recruitment. Prospective trajectories of eGFR were summarised with a linear slope for each patient, and patients with a loss >3 ml/min/1.73 m²/year were defined as rapid progressors. In non-fasting serum samples, following tryptic digestion, we measured 147 peptides by tandem mass spectrometry and tested them through linear/logistic regression models where biomarkers were evaluated independently. Significance was declared at p < 3.4 × 10⁻⁴.

Results: Median age was 55.7 years and diabetes duration 26.6 years. Over four-year follow-up, median annual change in eGFR was −1.17 ml/min/1.73 m²/year (interquartile range −3.12, 0.66), categorising 26.5% of the patients as rapid progressors. In models adjusted for age, sex, diabetes duration and eGFR, the T6 peptide of albumin, a highly conserved peptide and surrogate biomarker of serum albumin, was the only peptide significantly associated with prospective eGFR slopes (beta 0.14, 95% confidence interval, CI, 0.07, 0.21) and rapid progression (odds ratio 0.74, 95% CI 0.63, 0.87). Concentrations of the serum albumin T6 peptide are similar in normo- and microalbuminuric patients, but are reduced in macroalbuminuric individuals, presumably reflecting the renal losses.

Conclusions: Lower serum albumin T6 peptide is associated with a more rapid progression of renal function decline in patients with Type 1 diabetes.

Acknowledgement: SDRN Type 1 Bioresource Investigators.

A72 (P69)
Metabolic decompensation and altered body composition after short-term physical inactivity in first-degree relatives of patients with Type 2 diabetes vs healthy controls
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Aim: Physical inactivity is associated with obesity, insulin resistance and Type 2 diabetes. Here, we investigated the effects of short-term physical inactivity in first-degree relatives (FDR) of patients with Type 2 diabetes compared with healthy controls (CON).

Methods: Forty-five habitually active participants (16 FDR, 29 CON; age 36 ± 14 years) were assessed at baseline, after 14 days...