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### 1.4: A PROTEOMIC MARKER OF DIABETIC NEPHROPATHY IS ASSOCIATED WITH MORTALITY IN PATIENTS WITH TYPE 2 DIABETES

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Average cPP was  $36 \pm 7$  mmHg, PPamp  $1.57 \pm 0.13$ . cPP was positively associated with male sex, BSA, MAP, SI, and negatively with HR (47% of cPP variance explained). pPP was positively associated with male sex, BSA and SI (44% of pPP variance explained). PPamp was positively associated with age, HR and cf-PWV (17% of PPamp variance explained). Results did not change when BMI and height replaced BSA, iLVM replaced SI, and cr-PWV or PWV ratio (cfPWV/crPWV) replaced cf-PWV.

Anthropometric and hemodynamic factors differently impact on cPP, pPP and PPamp. HR and MAP are related to cPP, but not to pPP. HR, cf-PWV and age are all positively related to PPamp. These results could help in better elucidate the clinical relevance of some BP patterns frequently observed in adolescence.

**Table** independent determinants of cPP, pPP and PPamp. All the showed coefficients had  $p < 0.05$ .

	cPP	pPP	PPamp
	Standardized $\beta$	Standardized $\beta$	Standardized $\beta$
Male sex	0.33	0.40	—
BSA, m <sup>2</sup>	0.28	0.32	—
Heart rate, bpm	-0.21	—	0.32
Mean arterial pressure, mmHg	0.11	—	—
Stroke index, ml/m <sup>2</sup>	0.09	0.09	—
Carotid-femoral PWV, m/s	—	—	0.11
Age, years	—	—	0.10

#### 1.4

##### A PROTEOMIC MARKER OF DIABETIC NEPHROPATHY IS ASSOCIATED WITH MORTALITY IN PATIENTS WITH TYPE 2 DIABETES

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**Background:** The urinary proteomic classifier CKD273 has been found to predict diabetic nephropathy development in advance of microalbuminuria. Whether it is also a determinant of mortality and cardiovascular disease in patients with established albuminuria is unknown.

**Methods:** We studied 155 subjects with T2D, albuminuria (geometrical mean [IQR]: 85 [34;194] mg/24 hrs), controlled blood pressure ( $129 \pm 16/74 \pm 11$  mmHg) and preserved renal function (eGFR  $88 \pm 17$  ml/min/1.73 m<sup>2</sup>). Blood and urine samples were collected for measurement of estimated glomerular filtration rate (eGFR), urine albumin excretion (UAE), N-terminal pro-brain natriuretic peptide (NT-proBNP) and urinary proteomics (capillary electrophoresis coupled to mass spectrometry). Computed tomography imaging was performed to assess coronary artery calcium (CAC) score. Outcome data were collected through national disease registries over a 6 year follow up period.

**Results:** CKD273 correlated with UAE ( $r = 0.481$ ,  $p = < 0.001$ ), age ( $r = 0.238$ ,  $p = 0.003$ ), CAC score ( $r = 0.236$ ,  $p = 0.003$ ), NT-proBNP ( $r = 0.190$ ,  $p = 0.018$ ) and eGFR ( $r = 0.265$ ,  $p = 0.001$ ). On multiple regression only UAE ( $\beta = 0.402$ ,  $p < 0.001$ ) and eGFR ( $\beta = -0.184$ ,  $p = 0.039$ ) were statistically significant determinants. Twenty participants died during follow-up. CKD273 was a determinant of mortality (log rank [Mantel-Cox]  $p = 0.004$ ), and retained significance ( $p = 0.050$ ) after adjustment for age, sex, blood pressure, NT-proBNP and CAC score in a Cox regression model. Neither eGFR nor UAE were determinants of mortality in this cohort. **Conclusions:** A multidimensional biomarker can provide information on outcomes associated with its primary diagnostic purpose. Here we demonstrate that the peptidomics-based classifier CKD273 is associated with mortality in albuminuric people with T2D in even when adjusted for other established cardiovascular and renal biomarkers.

#### 1.5

##### DESPHOSPHO-UNCARBOXYLATED MATRIX GLA PROTEIN IS A NOVEL CIRCULATING BIOMARKER PREDICTING DETERIORATION OF RENAL FUNCTION IN THE GENERAL POPULATION

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**Background:** Recent studies showing an inverse association between estimated glomerular filtration rate (eGFR), a microvascular trait, and inactive desphospho-uncarboxylated matrix Gla protein (dp-ucMGP) support the hypothesis that after vitamin K dependent activation MGP is renoprotective, but were limited by their cross-sectional design.

**Methods:** In 1009 randomly recruited Flemish (50.6% women), we assessed the association between eGFR and plasma dp-ucMGP, using multivariable-adjusted analyses.

**Results:** From baseline to follow-up 8.9 years later (median), dp-ucMGP increased by 3.7%, whereas eGFR decreased by 4.05 ml/min/1.73 m<sup>2</sup> ( $P < 0.001$ ). In 938 participants with baseline eGFR  $\geq 60$  ml/min/1.73 m<sup>2</sup>, incidence of eGFR  $< 60$  ml/min/1.73 m<sup>2</sup> at follow-up was 8.0% vs. 4.1% in the top vs. the bottom half of baseline dp-ucMGP. For each doubling of baseline dp-ucMGP, eGFR at follow-up decreased by 1.36 ml/min/1.73 m<sup>2</sup> [95% confidence interval (CI) 0.55–2.17 ml/min/1.73 m<sup>2</sup>;  $P = 0.001$ ]. The hazard ratio expressing the risk of progression to eGFR  $< 60$  ml/min/1.73 m<sup>2</sup> was 1.67 (95% CI 1.16–2.41;  $P = 0.006$ ). The hazard ratio relating the presence of microalbuminuria at follow-up to baseline dp-ucMGP was 1.96 (95% CI 1.22–3.12;  $P = 0.005$ ).

**Conclusions:** In conclusion, circulating inactive dp-ucMGP, a biomarker of poor vitamin K status, predicts renal dysfunction. Possible underlying mechanisms include protection by activated MGP against calcification and inhibition of bone morphogenetic protein signaling pathway.

#### 1.6

##### PERIPHERAL AND CENTRAL AMBULATORY BLOOD PRESSURE IN RELATION TO ECG VOLTAGE

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**Background:** The heart ejects in the central elastic arteries. No previous study addressed the question whether ECG voltages are more closely associated with central than with peripheral blood pressure (BP).

**Methods:** Using the oscillometric Mobil-O-Graph 24h PWA monitor, we measured brachial, central BP and central hemodynamics over 24 hours in 177 men (mean age, 29.1 years), and linked to ECG voltages.

**Results:** From wakefulness to sleep, as documented by diaries, systolic/diastolic BP decreased by 11.7/13.1 mmHg peripherally and by 9.3/13.6 mmHg centrally, whereas pulse pressure (PP) increased by 4.3 mmHg. Over 24 hours and the awake and asleep periods, the peripheral-minus-central differences