Supplemental Materials

Synergistic effect of chronic kidney disease, neuropathy, and retinopathy on all-cause mortality in type 1 and type 2 diabetes: a 21-year longitudinal study.

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Supplemental Table 1. Baseline characteristics of the subgroup of study participants fully characterized for the presence of CKD, CAN, and DR.

Characteristics		*p* *
N	201	
Age, years – median [IQR]	58 [16]	0.790
Women – no. (%)	102 (50.8)	0.928
Body weight, kg – median [IQR]	77 [18]	0.578
Body mass index, kg/m2 – median [IQR]	27.7 [7.7]	0.747
Systolic blood pressure, mmHg – median [IQR]	137 [29.5]	0.499
Diastolic blood pressure, mmHg – median [IQR]	80 [12]	0.327
Diabetes mellitus – no. (%)		0.589
Type 2 Diabetes – no. (%)	52 (25.9)	
Type 1 Diabetes – no. (%)	149 (74.1)	
Duration of diabetes – median [IQR]	13 [15]	0.377
Smoke – no. (%)	60 (29.9)	0.542
Hypertension – no. (%)	108 (53.7)	0.705
Fasting glucose, mg/dl – median [IQR]	172 [100.5]	0.421
HbA1c, % – median [IQR]	9.1 [2.8]	0.073
Total cholesterol, mg/dl – median [IQR]	211 [69.5]	0.909
HDL cholesterol, mg/dl – median [IQR]	45 [13]	0.745
LDL cholesterol, mg/dl – median [IQR]	130 [62]	0.899
Triglycerides, mg/dl – median [IQR]	138 [95]	0.944
Creatinine, mg/dl – median [IQR]	0.88 [0.25]	0.837
mGFR, ml/min/1.73 m^2 – median [IQR]	100 [32]	0.962
eGFR, ml/min/1.73 m^2 – median [IQR]	85 [26.6]	0.912
Albuminuria, μg/min – median [IQR]	7.5 [14.2]	0.905
Glucose-lowering therapy – no. (%)	164 (81.6)	0.468
Oral agents – no. (%)	80 (39.8)	0.518
Insulin – no. (%)	107 (53.2)	0.499
Insulin, UI/die – median [IQR]	40 [18]	0.839
Lipid-lowering therapy – no. (%)	14 (7.0)	0.618
Anti-hypertensive therapy – no. (%)	108 (53.7)	0.716
ACEi/ARB – no. (%)	86 (46.5)	0.446
Beta-Blockers – no. (%)	9 (4.5)	0.549
Ca-Blockers – no. (%)	44 (21.9)	0.868
Alpha-Blockers – no. (%)	21 (10.5)	0.968

* For the difference with the whole study cohort.
Abbreviations: ACEi, angiotensin converting enzyme inhibitors; ARB, angiotensin II receptors blockers; CAN, cardiac autonomic neuropathy; CKD, chronic kidney disease; DR; diabetic retinopathy; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; mGFR, measured glomerular filtration rate.

Supplemental Table 2. Baseline characteristics of the study participants fully characterized for the presence of CKD, CAN, and DR stratified by the number of MVC.

Characteristics	No MVC	1 MVC	≥ 2 MVC	p
N (%)	74 (36.8)	72 (35.8)	55 (27.4)	
Age, years – median [IQR]	56 [18]	58 [18]	59 [13]	0.350
Women – no. (%)	34 (46.0)	33 (45.8)	26 (47.3)	0.575
Body weight, kg – median [IQR]	75.5 [17.7]	80.5 [20] [a]	75.6 [16.5]	0.048
Body mass index, kg/m2 – median [IQR]	26.2 [6.7]	29.2 [9.5] [a]	28.0 [5.7] [a]	0.023
Systolic blood pressure, mmHg – median [IQR]	130 [19]	140 [24] [a]	144 [32] [a]	0.009
Diastolic blood pressure, mmHg – median [IQR]	80 [9]	83 [12]	80 [16]	0.146
Diabetes mellitus – no. (%)				0.124
Type 2 Diabetes – no. (%)	16 (21.6)	16 (22.2)	20 (36.4)	
Type 1 Diabetes – no. (%)	58 (78.4)	56 (77.8)	35 (63.6)	
Duration of diabetes – median [IQR]	10 [12]	12 [16]	20 [16] [a, b]	<0.001
Smoke – no. (%)	25 (37.8)	20 (27.0)	15 (27.3)	0.820
Hypertension – no. (%)	29 (39.2)	41 (56.9)	38 (69.1)	0.003
Fasting glucose, mg/dl – median [IQR]	156.6 [89]	180 [39]	182 [120]	0.171
HbA1c, % – median [IQR]	8.6 [2.9]	9.3 [2.3]	9.5 [3.9] [a]	0.024
Total cholesterol, mg/dl – median [IQR]	216 [72]	218 [67]	203 [55]	0.421
HDL cholesterol, mg/dl – median [IQR]	44 [11]	46 [17]	45 [13]	0.733
LDL cholesterol, mg/dl – median [IQR]	133 [67]	131 [60]	128 [42]	0.937
Triglycerides, mg/dl – median [IQR]	143 [96]	136 [104]	135 [98]	0.722
Creatinine, mg/dl – median [IQR]	0.85 [0.23]	0.81 [0.28]	0.98 [0.34] [a, b]	0.001
mGFR, ml/min/1.73 m^2 – median [IQR]	107.0 [26.8]	98.0 [26.8] [a]	88.0 [51.0] [a, b]	0.002
eGFR, ml/min/1.73 m^2 – median [IQR]	89.9 [22.7]	85.6 [27.6]	74.7 [29.7] [a, b]	0.002
Albuminuria, µg/min – median [IQR]	5.0 [4.0]	8.8 [17.9] [a]	18.0 [45.9] [a, b]	<0.001
Glucose-lowering therapy – no. (%)	58 (78.4)	62 (86.1)	44 (80.0)	0.443
Oral agents – no. (%)	28 (37.8)	36 (50.0)	16 (29.1)	0.090
Insulin – no. (%)	34 (46.0)	33 (45.8)	40 (72.7)	0.003
Insulin, UI/die – median [IQR]	35 [16]	37 [18]	40 [16]	0.095
Lipid-lowering therapy – no. (%)	0 (0)	6 (8.3)	8 (14.6)	0.006
Anti-hypertensive therapy – no. (%)	29 (39.2)	41 (56.9)	38 (69.1)	0.014
ACEi/ARB – no. (%)	20 (27.0)	33 (45.8)	33 (60.0)	0.001
Beta-Blockers – no. (%)	1 (1.4)	4 (5.6)	4 (7.3)	0.220
Ca-Blockers – no. (%)	9 (12.2)	20 (27.8)	15 (27.2)	0.060
Alpha-Blockers – no. (%)	4 (5.4)	9 (12.5)	8 (14.6)	0.220

[a] p<0.05 vs No MVC; [b] p<0.05 vs 1 MVC.
* For the difference with the whole study cohort.
Abbreviations: ACEi, angiotensin converting enzyme inhibitors; ARB, angiotensin II receptors blockers; CAN, cardiac autonomic neuropathy; CKD, chronic kidney disease; DR; diabetic retinopathy; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; MVC, microvascular complication; mGFR, measured glomerular filtration rate.