

Supplemental Table S1. Baseline variables sorted by albuminuria and eGFR in type 1 diabetes
(n = 184)

	no DKD (n=134)	Low eGFR† group (n=9)	Albuminuria† † group (n=27)	Low eGFR and albuminuria group (n=14)	Overall (N=184)
Male	60 (45%)	4 (44%)	14 (52%)	8 (57%)	86 (47%)
Age (years)	50 (37-62)	67 (63-72) **	57 (48-62)	55 (47-66)	53 (40- 64)
BMI (kg/m ²)	22 (20-23)	25 (21-28) *	22 (20-25)	24 (22-25)	22 (20- 24)
Serum creatinine (mg/dL)	0.64 (0.55- 0.76)	1 (0.82-1.27) ***	0.69 (0.56- 0.81)	1.31 (0.96- 2.08) ***	0.68 (0.56- 0.81)
eGFR (mL/min/1.73m ²)	87 (75-100)	50 (43-54) ***	77 (70-90) *	40 (27-56) ***	82 (69- 97)
Total cholesterol (mg/dL)	194 (176- 213)	204 (176- 216)	192 (163-204)	185 (166-227)	193 (174- 212)
LDL cholesterol (mg/dL)	106 (89-118)	113 (107-118)	92 (83-111)	98 (78-107)	103 (86- 118)
HDL cholesterol (mg/dL)	69 (57-80)	68 (44-78)	60 (51-74)	58 (49-67) *	66 (55- 79)
Triglycerides (mg/dL)	74 (53-104)	109 (70-166) *	85 (75-162) **	98 (74-194) *	80 (58- 122)
HbA1c§ (%)	7.6 (6.8- 8.2)	6.9 (6.4-7.7)	8.5 (7.7-10.2) ***	7.3 (6.7-7.5)	7.6 (6.8- 8.3)
Uric acid (mg/dL)	4.2 (3.5-5)	5.1 (3.8-6.2)	4.6 (3.5-6.5)	6.4 (5.6-7.9) ***	4.5 (3.5- 5.2)
Systolic blood pressure (mmHg)	124 (113- 134)	128 (119- 139)	132 (126-148) *	130 (114-138)	126 (114- 135)
Diastolic blood pressure (mmHg)	70 (66-79)	72 (70-74)	80 (62-88)	76 (67-80)	71 (66- 80)
History of diabetic	11 (12%)	1 (17%)	8 (53%) ***	5 (50%) **	25 (20%)

Supplemental Table S2. Baseline variables sorted by albuminuria and eGFR in type 2 diabetes
(n = 2,154)

	no DKD (n=993)	Low eGFR† group (n=266)	Albuminuria† † group (n=481)	Low eGFR and albuminuria group (n=414)	Overall (N=2,154)
Male	636 (64%)	164 (62%)	314 (65%)	268 (65%)	1382 (64%)
Age (years)	63 (54-70)	71 (65-76) ***	62 (54-69)	66 (60-75) ***	65 (57- 72)
BMI (kg/m ²)	24 (22-27)	25 (23-28)	25 (22-28)	25 (23-28)	25 (22- 28)
Serum creatinine (mg/dL)	0.7 (0.6- 0.82)	1.02 (0.88- 1.14) ***	0.71 (0.6-0.83)	1.2 (1.03-1.6) ***	0.8 (0.65- 0.98)
eGFR (mL/min/1.73m ²)	78 (70-91)	52 (46-56) ***	77 (68-90)	44 (33-52) ***	70 (56- 83)
Total cholesterol (mg/dL)	181 (161- 206)	177 (156- 196) *	189 (166-213) **	187 (162-217) *	184 (161- 209) *
LDL cholesterol (mg/dL)	104 (85-124)	99 (79-115)**	104 (86-125)	97 (81-115)**	102 (84-122)
HDL cholesterol (mg/dL)	51 (42-61)	50 (42-61)	50 (42-60)	49 (42-62)	50 (42- 61)
Triglycerides (mg/dL)	117 (83- 172)	115 (88-162)	128 (88-182) **	124 (93-183) *	120 (86- 175)
HbA1c§ (%)	7.1 (6.5- 7.9)	7 (6.5-7.5)	7.5 (6.8-8.6) ***	6.9 (6.3-7.8) **	7.1 (6.5- 7.9)
Uric acid (mg/dL)	5 (4.3-6)	5.8 (5-6.6) ***	5.2 (4.3-6.2) **	6.1 (5.3-7.1) ***	5.3 (4.5- 6.3)
Systolic blood pressure (mmHg)	127 (118- 137)	126 (114- 138)	134 (121-146) ***	140 (126-152) ***	130 (120- 142)
Diastolic blood pressure (mmHg)	73 (67-81)	70 (64-76) ***	76 (69-84) ***	73 (65-80)	73 (67- 81)
History of diabetic	128 (23%)	43 (28%)	136 (53%) ***	209 (67%) ***	516 (41%)

Supplemental Table S3. The distribution of patients by eGFR and urinary albumin creatinine ratio (ACR) sorted by the type of diabetes

All patients	ACR<30 (mg/gCr)	≥ 30 (mg/gCr)	Total
eGFR ≥ 60 (mL/min/1.73m ²)	1,155 (48%)	514 (22%)	1,669 (70%)
eGFR <60 (mL/min/1.73m ²)	281 (12%)	435 (18%)	716 (30%)
Total	1,436 (60%)	949 (40%)	2,385
Type 1 diabetes			
eGFR ≥ 60 (mL/min/1.73m ²)	134 (73%)	27 (15%)	161 (88%)
eGFR <60 (mL/min/1.73m ²)	9 (5%)	14 (8%)	23 (12%)
Total	143 (78%)	41 (22%)	184
Type 2 diabetes			
eGFR ≥ 60 (mL/min/1.73m ²)	993 (50%)	481 (22%)	1,474 (68%)
eGFR <60 (mL/min/1.73m ²)	266 (13%)	414 (19%)	680 (32%)
Total	1,259 (58%)	895 (42%)	2,154
n (%)			

Supplemental Table S4. Risk factors of DKD by category after exclusion of patients from 2 hospitals that performed renal biopsies for all participants

Variables	Low eGFR group†		Albuminuria group††		Low eGFR and albuminuria group	
	OR	95%CI	OR	95%CI	OR	95%CI
Sex (female)	1.37	(0.81, 2.32)	0.98	(0.64, 1.51)	2.00	(1.22, 3.29)
Age (by 10 years)	2.69	(2.03, 3.58)	1.2	(1.01, 1.42)	1.89	(1.50, 2.40)
BMI (by 5 kg/m ²)	1.31	(0.95, 1.81)	1.23	(0.98, 1.56)	1.32	(0.99, 1.77)
Total cholesterol (by 10 mg/dL)	0.91	(0.83, 0.997)	0.93	(0.86, 0.999)	0.97	(0.90, 1.06)
HDL cholesterol (by 10 mg/dL)	0.99	(0.81, 1.21)	1.00	(0.86, 1.17)	0.99	(0.82, 1.18)
Triglyceride (by 10 mg/dL)	1	(0.97, 1.04)	1.01	(0.99, 1.04)	1.01	(0.97, 1.04)
HbA1c§ (%)	1.05	(0.81, 1.36)	1.30	(1.11, 1.51)	0.80	(0.61, 1.03)
Uric acid (mg/dL)	1.83	(1.48, 2.27)	1.11	(0.95, 1.31)	2.07	(1.69, 2.53)
SBP (by 10 mmHg)	-	-	1.33	(1.18, 1.50)	1.17	(1.02, 1.35)
DBP (by 10 mmHg)	1.06	(0.83, 1.34)	-	-	-	-
Diabetic retinopathy (yes/no)	1.23	(0.72, 2.10)	2.17	(1.46, 3.22)	3.45	(2.18, 5.48)

§NGSP, National Glycohemoglobin Standardization Program.

† eGFR < 60 mL/min/1.73m² and normoalbuminuria (ACR < 30 mg/gCr)

†† ACR ≥ 30 mg/gCr and normal eGFR (≥ 60 mL/min/1.73m²)

Note. Logistic regression analysis with each DKD group in contradistinction to no DKD group in order to find related risk factors.

Supplemental Table S5. Risk factors of diabetes kidney disease by category with LDL cholesterol as a variable instead of total cholesterol

Variables	Low eGFR group†		Albuminuria group††		Low eGFR and albuminuria group	
	OR	95%CI	OR	95%CI	OR	95%CI
Sex (female)	1.19	(0.72, 1.97)	0.97	(0.64, 1.48)	1.72	(1.07, 2.75)
Age (by 10 years)	2.71	(2.06, 3.57)	1.19	(1.01, 1.41)	1.85	(1.49, 2.30)
BMI (by 5 kg/m ²)	1.43	(1.04, 1.96)	1.28	(1.02, 1.60)	1.31	(1.00, 1.73)
LDL cholesterol (by 10 mg/dL)	0.96	(0.87, 1.05)	0.94	(0.87, 1.01)	0.98	(0.90, 1.06)
HDL cholesterol (by 10 mg/dL)	0.97	(0.82, 1.14)	0.95	(0.83, 1.08)	0.99	(0.86, 1.15)
Triglyceride (by 10 mg/dL)	0.99	(0.95, 1.02)	1.01	(0.98, 1.04)	1.02	(0.99, 1.04)
HbA1c§ (%)	1.02	(0.80, 1.30)	1.29	(1.11, 1.51)	0.76	(0.60, 0.98)
Uric acid (mg/dL)	1.86	(1.51, 2.28)	1.10	(0.94, 1.29)	2.01	(1.67, 2.43)
SBP (by 10 mmHg)	-	-	1.31	(1.16, 1.47)	1.23	(1.08, 1.40)
DBP (by 10 mmHg)	1.10	(0.87, 1.38)	-	-	-	-
Diabetic retinopathy (yes/no)	1.18	(0.70, 1.99)	2.11	(1.42, 3.13)	3.68	(2.36, 5.75)

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† eGFR < 60 mL/min/1.73m² and normoalbuminuria (ACR < 30 mg/gCr)

†† ACR ≥ 30 mg/gCr and normal eGFR (≥ 60 mL/min/1.73m²)

Note. Logistic regression analysis with each DKD group in contradistinction to no DKD group in order to find related risk factors.

Supplemental Table S6. Medication information by diabetic kidney disease category

	No DKD	Low eGFR group [†]	Albuminuria group ^{††}	Low eGFR and albuminuria group	Total
Oral antidiabetic drugs (%)	61%	70%	76%	65%	65%
P value	ref	0.15	0.012	0.86	(n=591)
Use insulin (%)	28%	34%	39%	47%	33%
P value	ref	0.24	0.01	<0.0001	(n=302)
Antidyslipidemic drugs (%)	42%	52%	60%	70%	50%
P value	ref	0.051	<0.0001	<0.0001	(n=448)
Antihypertensive drugs (%)	35%	49%	67%	87%	49%
P value	ref	0.0059	<0.0001	<0.0001	(n=450)
RAAS inhibitors (%)	30%	45%	59%	78%	44%
P value	ref	0.0033	<0.0001	<0.0001	(n=400)

[†] eGFR < 60 mL/min/1.73m² and normoalbuminuria (ACR < 30 mg/gCr)

^{††} ACR ≥ 30 mg/gCr and normal eGFR (≥ 60 mL/min/1.73m²)

Note. P value contradicted with no DKD by chi-square test. The population varied according to the number of medication data.

Supplemental Table S7. Distribution of variables at baseline for each analysis

	Participants for DKD prevalence (n=2,385)	Participants for early decliner (n=2,761)
Sex (Male)	1498 (63%)	1755 (64%)
Age (Years)	64 (55-71)†	66 (58-73)†
Type for diabetes (Type 2)	2154 (91%)	2659 (98%)
BMI (kg/m ²)	24.4 (22-27)†	24 (22-27)†
Total cholesterol (mg/dL)	185 (162-209)†	182 (160-205)†
LDL cholesterol (mg/dL)	102 (84-121)†	101 (83-119)
HDL cholesterol (mg/dL)	51 (43-63)†	52 (43-63)†
Triglycerides (mg/dL)	116 (83-170)†	115 (82-169)†
HbA1c§ (%)	7.1 (6.5-8.0)†	7.1 (6.6-7.8)†
Uric acid (mg/dL)	5.2 (4.4-6.2)†	5.3 (4.5-6.2)†
Systolic blood pressure (mmHg)	130 (119-142)†	128 (118-138)†
Diastolic blood pressure (mmHg)	73 (66-81)†	72 (65-80)†
eGFR (mL/min/1.73m ²)	70 (56-85)†	70 (57-82)†

The values are expressed in n (%) or median (IQR)†

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Supplemental Table S8. Yearly estimated glomerular filtration rate decrease classified by diabetes type and diabetic kidney disease category

	Type 1 diabetes (n=196)		Type 2 diabetes (n=2,299)	
	n	eGFR decline rate* (mL/min/1.73m ² /year)	n	eGFR decline rate* (mL/min/1.73m ² /year)
no DKD	139	-1.23 (-3.87 to 1.03)	1,154	-1.68 (-4.59 to 0.24)
Low eGFR group†	14	0.44 (-0.47 to 2.78)	337	-0.22 (-2.22 to 2.01)
Albuminuria group††	26	-2.18 (-4.34 to -0.35)	454	-2.68 (-6.15 to -0.56)
Low eGFR and albuminuria group	17	-1.73 (-3.16 to -0.22)	354	-1.08 (-3.95 to 0.79)

* Median (IQR)

† eGFR < 60 mL/min/1.73m² and normoalbuminuria (ACR < 30 mg/gCr)

†† ACR ≥ 30 mg/gCr and normal eGFR (≥ 60 mL/min/1.73m²)

Note. Patients were excluded whose measurement intervals were within 3 months.

Supplemental Table S9. Baseline risk factors of eGFR decline on multiple regression analysis and the rapidly lowering group (Group 1) by trajectory analysis with LDL cholesterol as a variable instead of total cholesterol

Variables	multiple regression analysis		trajectory analysis	
	Regression coefficient	95% confidence interval	Odds ratio	95% confidence interval
Sex (Female)	-0.063	-0.51, 0.38	1.32	0.99, 1.74
Age (by 10 years)	-0.45	-0.64, -0.26	1.64	1.45, 1.87
BMI (by 5 kg/m ²)	-0.04	-0.28, 0.19	0.97	0.89, 1.07
LDL cholesterol (by 10 mg/dL)	-0.016	-0.092, 0.060	1.01	0.96, 1.05
HDL cholesterol (by 10 mg/dL)	0.10	-0.033, 0.24	0.95	0.87, 1.04
Triglycerides (by 10 mg/dL)	-0.029	-0.055, -0.0031	1.03	1.01, 1.05
HbA1c§ (%)	-0.056	-0.24, 0.12	1.08	0.96, 1.20
Uric acid (mg/dL)	0.064	-0.13, 0.25	1.05	0.93, 1.18
Systolic blood pressure (by 10 mmHg)	-0.17	-0.29, -0.051	1.04	0.96, 1.12
ACR (by 10 mg/gCr)	-0.019	-0.026, -0.011	1.01	1.01, 1.02
eGFR (by 10 mL/min/1.73m ²)	-0.81	-0.98, -0.65	2.39	2.14, 2.68

§NGSP, National Glycohemoglobin Standardization Program.

Note. Calculated by multiple regression analysis as to yearly change of eGFR to identify the baseline risk factors weighting by the square of follow-up period.

Calculated by multiple logistic regression analysis in contradistinction to moderate lowering group (group2).

Supplemental Table S10. Posterior probability of each group calculated on trajectory analysis

Mean values of posterior probability with each group			
Groups patients really belong to	Group 1	Group 2	Group 3
Group 1	0.86	0.14	0.0006
Group 2	0.055	0.88	0.070
Group 3	0.00015	0.15	0.85

Supplemental Table S11. Risk factors of the gradually rising group (Group 3) by trajectory analysis

Variables	Odds ratio	95% confidence interval
Sex (Female)	1.19	0.88, 1.61
Age (by 10 years)	0.83	0.73, 0.94
BMI (by 5 kg/m ²)	0.997	0.95, 1.04
Total cholesterol (by 10 mg/dL)	0.96	0.91, 1.00
HDL cholesterol (by 10 mg/dL)	1.07	0.97, 1.20
Triglycerides (by 10 mg/dL)	1.00	0.98, 1.02
HbA1c§ (%)	0.98	0.85, 1.13
Uric acid (mg/dL)	1.02	0.90, 1.15
eGFR (by 10 mL/ml/1.73m ²)	0.73	0.64, 0.84
ACR (by 10 mg/gCr)	0.99	0.97, 0.998
Systolic blood pressure (by 10 mmHg)	0.93	0.85, 1.02

§NGSP, National Glycohemoglobin Standardization Program.

Note. Calculated by multiple logistic regression analysis in contradistinction to moderate lowering group (Group2).