

Table S1. Baseline clinical and pathological characteristics among patients with and without diabetic macular edema

	Total (n=232)	No DME (n=189)	DME (n=43)	P-value
Clinical characteristics				
Age (year)	59 (50, 67)	60 (51, 67)	56 (44, 63)	0.060
Male (%)	78	78	74	0.58
BMI (kg/m ²)	24 (22, 27)	24 (22, 27)	24 (21, 27)	0.62
Diabetes duration (year)	14 (10, 21)	15 (10, 22)	13 (9, 18)	0.28
Past history of CVD (%)	24	24	21	0.64
Ever having Smoked (%)	61	61	62	0.95
RAAS inhibitors use (%)	66	65	70	0.52
Glucose lowering agents use (%)	81	79	88	0.15
Statin use (%)	29	29	31	0.84
Systolic blood pressure (mmHg)	145 (132, 160)	143 (131, 158)	153 (137, 170)	0.012
Diastolic blood pressure (mmHg)	80 (72, 90)	80 (72, 90)	82 (77, 90)	0.13
Hemoglobin A1c (%)	7.3 (6.4, 8.9)	7.3 (6.4, 8.9)	7.2 (6.3, 9.1)	0.98
(mmol/mol)	56 (46, 74)	56 (46, 74)	55 (45, 76)	0.98
Total cholesterol (mmol/L)	209 (174, 253)	206 (171, 250)	214 (190, 261)	0.053
Triglycerides (mmol/L)	157 (114, 215)	156 (114, 214)	171 (117, 230)	0.61
LDL-C (mmol/L)	125 (100, 171)	121 (99, 166)	142 (121, 180)	0.025
HDL-C (mmol/L)	40 (33, 50)	39 (32, 49)	43 (35, 57)	0.34
Uric acid (mg/dL)	6.6 (5.6, 7.5)	6.6 (5.6, 7.5)	6.5 (5.6, 7.9)	0.67
eGFR (mL/min per 1.73 m ²)	39 (25, 61)	44 (27, 62)	33 (16, 54)	0.014
UACR (g/g)	1.4 (0.5, 3.2)	1.2 (0.5, 2.7)	1.9 (1.2, 4.4)	0.0086
Pathological characteristics				
RPS DN Classification				0.26
Class I	6	7	0	
Class IIa	20	23	7	
Class IIb	28	29	23	
Class III	32	27	54	
Class IV	14	14	16	
IFTA				0.16
0	6	7	2	
1	28	30	16	
2	33	31	42	
3	33	32	40	
Interstitial inflammation				
0	10	11	5	0.44
1	77	76	81	
2	13	13	14	
Arteriolar hyalinosis				0.084
0	6	6	2	
1	13	15	5	
2	81	79	93	
Arteriosclerosis				0.79
0	7	6	9	
1	47	48	47	
2	46	46	44	
Diffuse				0.061
0	6	7	0	
1	15	19	0	
2	33	33	35	
3	46	41	65	
Exudative	66	60	90	0.012
Subendothelial space widening	67	65	80	0.20
Mesangiolysis/microaneurysm	46	41	65	0.053
Perihilar neovascularization	81	77	95	0.069

BMI, body mass index; RAAS, renin-angiotensin-aldosterone system blockade; LDL-C, low-density-lipoprotein cholesterol; HDL-C, high-density-lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; UACR, urine albumin to creatinine ratio. RPS DN classification, Renal Pathology Society classification of diabetic nephropathy; I; Mild or nonspecific light microscopy changes and electron microscopy-proven glomerular membrane thickening; IIa; Mild mesangial expansion; IIb, Severe mesangial expansion; III; Nodular sclerosis (Kimmelstiel-Wilson lesion); IV, Advanced diabetic glomerulosclerosis; IFTA, interstitial fibrosis and tubular atrophy. Data are expressed as the mean (standard deviation), median (25th, 75th percentiles), or percentage.

Table S2. Correlation between retinal findings and renal lesions

	Microaneurysms	Retinal dot and blot hemorrhages	Hard exudates or cotton wool spots	Intraretinal microvascular abnormality	Neovascularization	Vitreous or preretinal hemorrhages	Diabetic macular edema	Diffuse lesions	Exudative lesions	Nodular lesions	IFTA	Interstitial inflammation	Arteriolar hyalinosis	Arterioatherosclerosis	Perihilar neovascularization
Microaneurysms	1.00														
Retinal dot and blot hemorrhages	-0.18*	1.00													
Hard exudates or cotton wool spots	-0.13	0.51***	1.00												
Intraretinal microvascular abnormality	0.10	0.14*	-0.11	1.00											
Neovascularization	-0.07	0.25***	0.28**	0.07	1.00										
Vitreous or preretinal hemorrhages	-0.11	0.22**	0.23**	0.02	0.11	1.00									
Diabetic macular edema	-0.13	0.29***	0.25**	0.05	0.30***	0.20***	1.00								
Diffuse lesions	0.11	0.50***	0.36**	0.14	0.22*	0.10	0.25*	1.00							
Exudative lesions	0.00	0.23*	0.23*	-0.19	0.08	0.17	0.25*	0.49**	1.00						
Nodular lesions	-0.05	0.27**	0.27*	-0.14	-0.07	0.17	0.16	0.60**	0.38**	1.00					
IFTA	0.10	0.25***	0.23**	0.02	0.12	0.14	0.13*	0.61**	0.55**	0.41**	1.00				
Interstitial inflammation	-0.04	0.18*	0.20*	0.00	0.02	0.12	0.06	0.27*	0.41**	0.07	0.50**	1.00			
Arteriolar hyalinosis	0.07	0.22***	0.10	0.13	-0.01	0.01	0.13*	0.47**	0.34**	0.29*	0.48**	0.41***	1.00		
Arterioatherosclerosis	0.11	0.08	0.01	0.01	0.02	0.05	-0.03	0.24*	0.21*	0.25	0.38**	0.23***	0.30**	1.00	
Polar vasculosis	-0.05	0.32*	0.05	0.07	0.09	0.19	0.18	0.48**	0.27**	0.28*	0.35**	0.11	0.29**	0.14	1.00

Spearman's Correlation coefficients, r , between the International Clinical Diabetic Retinopathy Disease Severity Scale and renal lesions, were obtained using Spearman's correlation rank test. * P -value<0.05; ** P -value<0.01; *** P -value<0.001.

Table S3. Adjusted Risk for ESKD, CVD, and all-cause death, among patients with diabetic macular edema, as compared with patients with no diabetic macular edema

Model	ESKD	CVD	All-cause death
	DME	DME	DME
1	1.99 (1.30-3.05) <i>P</i> =0.002	1.27 (0.63-2.56) <i>P</i> =0.51	0.64 (0.27-1.52) <i>P</i> =0.31
2	1.94 (1.25-2.99) <i>P</i> =0.003	1.31 (0.64-2.67) <i>P</i> =0.13	0.74 (0.30-1.78) <i>P</i> =0.50
3	1.11 (0.70-1.75) <i>P</i> =0.66	1.38 (0.65-2.92) <i>P</i> =0.40	0.59 (0.23-1.50) <i>P</i> =0.26

DME, diabetic macular edema; ESKD, end-stage kidney disease; CVD, cardiovascular disease. Hazard ratios (95% confidence interval) and *P*-values were determined for demographic and laboratory characteristics by univariable and multivariable Cox proportional hazard models. Model 1: univariable (no diabetic retinopathy as reference). Model 2: model 1 + adjusted for demographic characteristics (age, gender, BMI, diabetic duration, ever having smoked and systolic blood pressure). Model 3: model 2 + adjusted for laboratory characteristics (hemoglobin A1c, triglycerides, eGFR, and UACR).