

Supplementary material

Title: The role of glomerular epithelial injury in kidney function decline in patients with diabetic kidney disease in the TRIDENT cohort

Running headline: Pathological descriptors in patients with diabetes mellitus

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Supplementary Table S1. Correlation analysis between pathological parameters and clinical characteristics.

Variables		Age (yr)	Duration of DM (yr)	BMI- Baseline (Kg/m²)	SBP- Baseline (mmHg)	DBP- Baseline (mmHg)	HbA1C (%)	eGFR- Baseline (ml/min/1.73 m²)	eGFR Change (%/yr)	UPCR- Baseline (mg/g)	UPCR fold change (/yr)
KW nodules	r	-0.168	0.054	-0.072	0.046	-0.042	0.031	-0.249	-0.142	0.338	-0.161
	P value	0.192	0.678	0.578	0.72	0.744	0.811	0.051	0.271	0.007	0.212
RPS DN Class	r	-0.152	0.043	-0.052	0.052	0.116	0.086	-0.262	-0.234	0.295	-0.022
	P value	0.239	0.74	0.686	0.687	0.37	0.508	0.04	0.067	0.02	0.865
Segmental Sclerosis	r	0.065	0.03	-0.291	-0.022	0.076	-0.243	-0.031	-0.031	0.237	0.081
	P value	0.618	0.815	0.022	0.864	0.558	0.057	0.809	0.808	0.064	0.53
Global Sclerosis	r	-0.03	0.093	0.008	0.115	0.084	-0.049	-0.339	-0.36	0.271	0.055
	P value	0.817	0.473	0.951	0.374	0.515	0.704	0.007	0.004	0.033	0.669
Glomerular Epithelial Hypertrophy	r	-0.177	-0.021	-0.161	0.014	0.002	-0.066	0.031	-0.159	0.222	-0.089
	P value	0.169	0.871	0.211	0.916	0.987	0.608	0.814	0.217	0.083	0.489
Glomerular Epithelial Hyperplasia	r	-0.228	0.049	-0.145	0.091	0.027	-0.014	-0.058	-0.209	0.204	0.015
	P value	0.075	0.708	0.261	0.482	0.834	0.913	0.655	0.103	0.112	0.906
Mesangiolysis	r	-0.357	-0.085	0.073	0.155	0.053	0.152	-0.181	-0.397	0.503	-0.117
	P value	0.004	0.511	0.57	0.228	0.684	0.239	0.16	0.001	0	0.366
Insudative Lesions	r	-0.207	-0.046	0.041	0.096	0.085	0.123	-0.203	-0.385	0.435	-0.062
	P value	0.107	0.722	0.75	0.456	0.513	0.34	0.114	0.002	0	0.635
Interstitial Fibrosis (%)	r	-0.2	0.112	-0.104	-0.011	0.14	-0.006	-0.392	-0.284	0.265	0.083
	P value	0.12	0.387	0.421	0.934	0.277	0.964	0.002	0.025	0.037	0.521

Interstitial Lymphocytes	r	-0.153	0.164	-0.17	-0.048	0.053	0.131	-0.378	-0.22	0.235	-0.045
	P value	0.235	0.202	0.188	0.711	0.682	0.311	0.002	0.085	0.066	0.729
Arteriolar Hyalinosis	r	-0.123	0.013	0.008	0.092	-0.048	0.115	-0.326	-0.107	0.403	-0.118
	P value	0.34	0.923	0.951	0.479	0.713	0.374	0.01	0.407	0.001	0.359
Intimal Fibrosis	r	0.228	0.012	-0.028	0.36	-0.145	0.05	-0.322	-0.05	0.501	-0.232
	P value	0.075	0.927	0.83	0.004	0.26	0.698	0.011	0.699	0	0.069
Average GBM Thickness (nm)	r	-0.143	-0.175	-0.004	-0.071	-0.02	-0.066	0.063	-0.2	0.33	-0.13
	P value	0.269	0.174	0.975	0.581	0.875	0.608	0.626	0.119	0.009	0.312
GBM Lamina Densa Remodeling	r	0.075	0.139	-0.19	0.056	-0.051	-0.086	-0.18	0.094	-0.143	0.188
	P value	0.561	0.281	0.139	0.667	0.694	0.504	0.161	0.468	0.269	0.143
GBM Duplication	r	-0.068	0.139	-0.025	0.162	-0.019	-0.214	-0.003	-0.232	0.174	0.086
	P value	0.598	0.283	0.847	0.21	0.882	0.094	0.981	0.07	0.176	0.507
Average FPW (µm)	r	0.019	-0.093	0.009	0.033	0.087	-0.113	-0.03	-0.254	0.374	-0.066
	P value	0.885	0.474	0.946	0.798	0.5	0.382	0.817	0.047	0.003	0.609
Foot Process Effacement (%)	r	0.071	0.122	-0.15	0.005	-0.073	-0.184	-0.112	-0.157	0.371	-0.012
	P value	0.585	0.346	0.246	0.968	0.572	0.152	0.386	0.222	0.003	0.924
Endothelial Fenestration Loss	r	0.061	0.045	-0.202	0.12	-0.087	0.172	-0.217	-0.105	0.109	0.03
	P value	0.64	0.731	0.115	0.354	0.501	0.18	0.091	0.417	0.401	0.815
Mesangial Hyaline	r	-0.118	0.083	-0.219	-0.036	0.047	-0.131	-0.286	-0.109	0.173	0.265

	P										
	value	0.359	0.524	0.087	0.782	0.715	0.311	0.024	0.399	0.18	0.037
Mesangial	r										
Matrix											
Increase		-0.15	0.114	0.041	-0.012	-0.1	0.061	-0.199	-0.077	0.353	0.006
	P										
	value	0.244	0.378	0.753	0.929	0.442	0.637	0.121	0.552	0.005	0.961

Descriptors are shown by different colors: Glomerular-LM descriptors (red), interstitial descriptors (blue), vasculature descriptors (yellow), and glomerular-EM descriptors (green). Correlation analysis was performed using Spearman test. KW nodules; Kimmelsteil-Wilson nodules, RPS DN class; Renal Pathology Society diabetic nephropathy class, GBM; glomerular basement membrane, FPW; foot process width.

Supplementary Table S2. Univariate Cox Proportional Hazard analysis of clinical and pathological findings in ESKD progression.

Variables	HR	95%CI	P value	P value for the proportionality of Cox model
Age	0.97	0.94-1.01	0.22	0.93
Gender				
Female	Ref	-	-	
Male	1.1	0.38-3.14	0.85	0.42
Race				
Non-AA	Ref	-	-	
AA	0.77	0.27-2.21	0.63	0.67
Duration of DM (yr)	1.01	0.97-1.05	0.57	0.86
HbA1C (%)	1.16	0.88-1.54	0.28	0.29
eGFR-Baseline (ml/min/1.73m²)	0.94	0.9-0.98	0.006	0.002
UPCR-Baseline (mg/g)	1.04	1.01-1.08	0.007	0.16
Glomerular Epithelial Hyperplasia				
0	Ref	-	-	
1	4.77	1.68-13.55	0.003	0.68
Interstitial Fibrosis (%)				
0-25	Ref	-	0.005	
25-50	0.18	0.01-2.09	0.17	0.34
50-75	1.85	0.37-9.2	0.45	
75-100	5.37	1.12-25.68	0.03	
GBM Lamina Densa Remodeling				
0	Ref	-	-	
1	0.24	0.06-0.91	0.03	0.1
2	-	-	0.98	
3	-	-	0.93	
Clusters				
1	Ref	-	0.02	
2	17.89	2.13-149.79	0.008	0.43
3	9.81	1.25-76.79	0.03	

All pathological descriptors as well as clusters were examined using cox proportional hazard analysis; however, only significant associations are shown in the table. Baseline demographic and clinical features are shown in the table as well, because they were used for adjustment in the final model except eGFR-baseline due to lack of Cox proportionality. HR; hazard ratio, CI; confidence interval, AA; African-American, DM; diabetes mellitus, HbA1C; hemoglobin A1C, eGFR; estimated glomerular filtration rate, UPCR; urine protein to creatinine ratio, GBM; glomerular basement membrane.