

Title Page

OCT-based biomarkers are associated with systemic inflammation in patients with treatment-naïve diabetic macular edema

Jingxin Zhou¹, Siyuan Song¹, Yi Zhang², Kai Jin^{1*}, and Juan Ye^{1*}

¹ Department of Ophthalmology, the Second Affiliated Hospital of Zhejiang University, School of Medicine, Hangzhou 310009, China.

² Department of Ophthalmology, the First Affiliated Hospital of Zhejiang Chinese Medical University, Zhejiang Provincial Hospital of Traditional Chinese Medicine, Hangzhou 310009, China.

*Corresponding Author: Juan Ye (yejuan@zju.edu.cn), Kai Jin (jinkai@zju.edu.cn).

Supplementary material

Supplementary material

Table S1 Comparison of clinical characteristics between subjects with different IRC size.

	Cyst size			P value
	Mild (n=17)	Moderate (n=37)	Severe (n=28)	
Age (years)	64.94±9.70	63.35±9.38	57.58±11.78	0.034
DM Duration (years)	10.06±4.47	11.32±4.54	12.00±4.22	0.364
BCVA (mean ± SD)	0.20±0.22	0.28±0.20	0.42±0.27	0.008
DR severity (n)				0.169
Mild NPDR	5	5	2	
Moderate NPDR	5	7	10	
Severe NPDR	2	5	17	
PDR	5	10	9	
SII	467.27±181.66	543.19±303.66	610.79±238.96	0.092
NLR	2.42±0.79	2.76±1.24	2.93±1.13	0.331
PLR	115.55±42.00	128.89±52.80	135.23±37.55	0.256

Table S2 Comparison of clinical characteristics between subjects with different ELM/EZ integrity.

	ELM/EZ integrity			P value
	Intact (n=33)	Disrupted (n=42)	Absent (n=7)	
Age (years)	61.63±10.36	61.88±10.43	61.06±14.55	0.981
DM Duration (years)	11.12±4.07	11.64±4.67	10.00±4.76	0.639
DR severity (n)				0.947
Mild NPDR	5	7	0	
Moderate NPDR	9	11	2	
Severe NPDR	9	12	3	
PDR	10	12	2	
BCVA (mean ± SD)	0.05±0.04	0.33±0.21	0.20±0.23	<0.001
SII	515.42±257.54	565.57±255.56	654.44±322.08	0.476
NLR	2.68±1.14	2.74±1.12	3.12±1.18	0.660
PLR	125.18±44.34	127.61±46.40	147.01±52.92	0.622

Supplementary material

Table S3 Comparison of clinical characteristics between subjects with different DRIL presence.

	DRIL		P value
	Intact (n=70)	Disrupted (n=12)	
Age (years)	61.43 ± 10.81	63.35 ± 9.83	0.567
DM Duration (years)	11.13 ± 4.32	12.17 ± 5.06	0.461
DR severity (n)			0.704
Mild NPDR	10	2	
Moderate NPDR	20	2	
Severe NPDR	19	5	
PDR	21	3	
BCVA	0.08 ± 0.07	0.32 ± 0.23	<0.001
SII	557.08 ± 272.87	528.98 ± 191.17	0.963
NLR	2.77 ± 1.19	2.58 ± 0.62	0.911
PLR	128.21 ± 46.02	128.78 ± 47.32	0.985

Table S4 Comparison of clinical characteristics between subjects with different HRF number quartile.

	Hyperreflective foci				P value
	Quartile 1 (n=20)	Quartile 2 (n=21)	Quartile 3 (n=21)	Quartile 4 (n=20)	
Age (years)	62.49 ± 8.51	61.97 ± 14.28	58.32 ± 8.53	64.22 ± 9.92	0.343
DM Duration (years)	11.40 ± 3.79	10.57 ± 4.12	9.52 ± 3.87	13.80 ± 4.95	0.013
DR severity (n)					<0.001
Mild NPDR	6	4	2	0	
Moderate NPDR	10	5	5	2	
Severe NPDR	2	10	8	4	
PDR	2	2	6	14	
BCVA	0.21 ± 0.17	0.31 ± 0.26	0.31 ± 0.24	0.30 ± 0.25	0.388
SII	430.57 ± 120.82	482.78 ± 175.16	533.18 ± 247.38	769.85 ± 330.94	0.001
NLR	2.38 ± 0.75	2.4949 ± 0.78	2.56 ± 1.17	3.57 ± 1.33	0.003
PLR	115.95 ± 45.69	109.64 ± 35.77	122.94 ± 36.05	165.84 ± 46.10	<0.001

Supplementary material

Table S5 Comparison of clinical characteristics between subjects with different SRF presence.

	Subretinal fluid		P value
	Absent (n=51)	Present (n=31)	
Age (years)	63.81 ± 10.32	58.27 ± 10.40	0.021
DM Duration (years)	11.24 ± 4.26	11.39 ± 4.72	0.881
DR severity (n)			0.102
Mild NPDR	10	2	
Moderate NPDR	16	6	
Severe NPDR	14	10	
PDR	11	13	
BCVA	0.24 ± 0.21	0.31 ± 0.24	0.164
SII	501.73 ± 205.54	637.27 ± 320.49	0.022
NLR	2.59 ± 0.93	3.00 ± 1.37	0.203
PLR	118.86 ± 42.37	143.80 ± 47.96	0.021

Table S6 Comparison of clinical characteristics between subjects with different vitreomacular condition.

	Vitreomacular condition					P value
	No adhesion (n=32)	IVD (n=23)	CVD (n=5)	VMT (n=5)	ERM (n=17)	
Age (years)	62.05 ± 11.00	58.42 ± 9.93	57.26 ± 9.07	63.34 ± 9.28	66.35 ± 10.71	0.165
Duration (years)	11.63 ± 4.53	11.04 ± 4.26	11.40 ± 3.65	11.60 ± 4.34	10.88 ± 5.05	0.981
DR severity (n)						0.975
Mild NPDR	6	2	0	1	3	
Moderate NPDR	8	7	3	0	4	
Severe NPDR	9	6	2	2	5	
PDR	9	8	0	2	5	
BCVA	0.17 ± 0.18	0.28 ± 0.19	0.41 ± 0.36	0.27 ± 0.22	0.32 ± 0.24	0.063
SII	537.20 ± 218.86	565.99 ± 303.21	522.22 ± 236.39	570.38 ± 191.35	568.96 ± 320.93	0.990
NLR	2.69 ± 0.94	2.73 ± 1.28	2.61 ± 1.69	2.63 ± 0.33	2.95 ± 1.27	0.835
PLR	127.56 ± 46.29	123.91 ± 35.57	121.97 ± 33.30	132.87 ± 52.00	136.10 ± 0.96	0.996

Supplementary material

Table S7. Subgroup analysis result based on SRF presence.

	HRF (SRF absence)				HRF (SRF presence)			
	Univariable		Multivariable		Univariable		Multivariable	
	β coefficient	P value	β coefficient	P value	β coefficient	P value	β coefficient	P value
Age	0.152	0.286	/	/	0.229	0.215	/	/
DM Duration	0.181	0.203	/	/	0.443	0.012	0.365	0.015
DR Severity	0.492	0.001	0.376	0.005	0.461	0.009	0.172	0.288
BCVA	0.104	0.472	/	/	0.140	0.452	/	/
Cyst Size	0.261	0.795	/	/	0.272	0.787	/	/
ELM/EZ	0.314	0.025	0.256	0.057	0.246	0.181	/	/
DRIL	-0.195	0.846	/	/	0.026	0.890	/	/
HRF	/	/	/	/	/	/	/	/
SRF	/	/	/	/	/	/	/	/
VM	-0.064	0.658	/	/	0.231	0.212	/	/
SII (ln)	0.372	0.007	0.372	0.007	0.505	0.004	0.520	0.001
NLR (ln)	0.309	0.027	0.509	0.073	0.518	0.003	-0.110	0.700
PLR (ln)	0.233	0.100	/	/	0.549	0.001	0.142	0.526

Table S8. Subgroup analysis result based on DM duration.

	HRF (DM duration no more than 10 years)				HRF (DM duration over 10 years)			
	Univariable		Multivariable		Univariable		Multivariable	
	β coefficient	P value	β coefficient	P value	β coefficient	P value	β coefficient	P value
Age	-0.018	0.905	/	/	0.023	0.892	/	/
DM Duration	/	/	/	/	/	/	/	/
DR Severity	0.468	0.042	0.317	0.017	0.560	<0.001	0.357	0.009
BCVA	0.201	0.180	/	/	0.090	0.606	/	/
Cyst Size	0.296	0.045	0.121	0.344	-0.204	0.232	/	/
ELM/EZ	0.232	0.121	/	/	0.294	0.082	0.148	0.230
DRIL	-0.024	0.873	/	/	-0.040	0.815	/	/
HRF	/	/	/	/	/	/	/	/
SRF	0.328	0.026	0.119	0.364	0.511	0.001	0.335	0.010
VM	0.123	0.820	/	/	0.100	0.560	/	/
SII (ln)	0.451	0.002	0.430	0.002	0.450	0.006	0.137	0.542
NLR (ln)	0.309	0.037	-0.080	0.686	0.526	0.001	0.335	0.015
PLR (ln)	0.307	0.038	-0.080	0.599	0.557	<0.001	0.046	0.789

Supplementary material

Table S9. Subgroup analysis result based on ELM/EZ integrity.

	HRF (ELM/EZ intact)				HRF (ELM/EZ disrupted)				HRF (ELM/EZ absent)			
	Univariable		Multivariable		Univariable		Multivariable		Univariable		Multivariable	
	β	P value	β	P value	β	P value	β	P value	β	P value	β	P value
Age	-0.022	0.903	/	/	0.119	0.453	/	/	0.073	0.876	/	/
DM Duration	0.191	0.288	/	/	0.351	0.023	0.172	0.261	0.442	0.321	/	/
DM severity	0.613	<0.001	0.454	0.003	0.523	<0.001	0.351	0.026	0.632	0.555		
BCVA	0.247	0.166	/	/	0.070	0.663	/	/	0.532	0.219	/	/
Cyst Size	0.160	0.374	/	/	-0.247	0.115	/	/	0.510	0.243	/	/
ELM/EZ	/	/	/	/	/	/	/	/	/	/	/	/
DRIL	/	/	/	/	-0.181	0.250	/	/	-0.134	0.775	/	/
HRF	/	/	/	/	/	/	/	/	/	/	/	/
SRF	0.547	0.001	0.270	0.061	0.296	0.057	/	/	0.549	0.202	/	/
VM	0.153	0.397	/	/	-0.210	0.182	/	/	0.736	0.059	/	/
SII (ln)	0.469	0.006	0.404	0.007	0.398	0.009	0.146	0.428	0.754	0.050	0.370	0.237
NLR (ln)	0.317	0.072	/	/	0.423	0.005	0.181	0.425	0.748	0.053	/	/
PLR (ln)	0.212	0.235	/	/	0.496	0.001	0.326	0.038	0.808	0.028	0.866	0.012