Hemorheological Alterations in Patients with Diabetic Nephropathy

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Objectives:

Hemorheologic alterations or changes in blood viscosity have been suggested to play a role in the pathogenesis of diabetic microvascular complications. Increased plasma viscosity correlates to the progression of CAD, PAD and many conventional CV risk factors, and significant differences in the degree of RBC deformability are observed in diabetes patients compared to healthy control and diabetes patients with chronic renal disease or end stage renal disease compared to those with normal renal function. Hemorheologic changes have been reported in patients with new onset diabetes and may precede the development of diabetic microangiopathy. We aimed to assess the hemorheologic alterations in patients with type 2 diabetes at different stages of CKD, to compare hemorheologic parameters with urine albumin creatinine ratio, and assess its possible role as an early marker of diabetic nephropathy

Methods:

Subjects

One hundred-five patients with type 2 diabetes were divided into four groups according to glomerular filtration rate (GFR) and urinary albumin creatinine ratio (ACR).

Anthropometric & biochemical measurements: fasting blood samples and first morning voided urine

Hemorheologic measurements: microfluidic hemorheometer (point of care testing)

- Deformability measurements: (L − W) / (L + W) (L: major axis, W minor axes of ellipse)

  Deformability: Elongation index (EI) in RBCs exposed to shear stress (3 Pa)

- Critical shear stress (CSS): minimum shear stress required to disperse RBC aggregates measured by transient microfluidic technique using native whole blood

- Erythrocyte aggregation: Perfused blood samples into a microchip, and a magnetic rotating mechanism stirs the suspension in order to induce shear flow to disaggregate the RBCs. A light signal transmitted through the blood sample is detected by a photodiode, and data are analyzed by computer .

Conclusions:

1.Several hemorheologic parameters including a novel index Fibrinogen/EI at 3 Pa, showed significant differences among different stages of CKD and diabetic nephropathy in patients with type 2 diabetes.

2.Hemorheologic alterations showed close linear relationships to urinary albumin creatinine ratio.

3.It was valid in differentiating patients with mild CKD from normal renal function as well as microalbuminuria from normal.

4.With the accumulation of clinical data and the establishment of appropriate reference values, hemorrheologic parameters may be used as screening tools for renal dysfunction and diabetic nephropathy

Results:

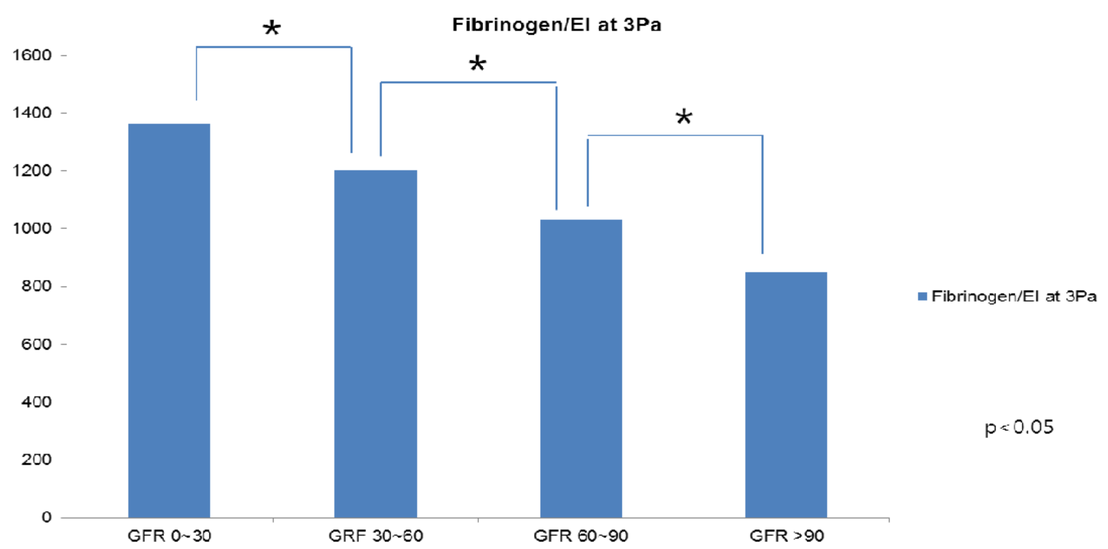
Baseline characteristics

	GFR > 90 mL/min/1.73 m² (N=73)	GFR 60~90 mL/min/1.73 m² (N=19)	GFR 30~60 mL/min/1.73 m² (N=10)	GFR < 30 mL/min/1.73 m² (N=3)	P-value
Age, years	57.8	62.5	56.7	56.3	0.124
Sex (female, %)	41.1	47.4	50	0	0.44
BMI (kg/m²)	24.24	25.4	25.79	27.2	0.124
Systolic BP (mmHg)	122	123	131.5	147.6	**<0.001**
Diastolic BP (mmHg)	73	74	75.9	80.3	0.287
HbA1c(%) (mmol/mol)	7.4 (57)	9.2 (77)	7.9 (53)	8.9 (63)	0.22
FPG (mg/dL)	149	216.95	151	212	0.23
Urine ACR (mg/mmol)	9.86	272.63	2231.2	3474	**<0.001**
T. cholesterol (mg/dL)	121.99	171.16	206.9	153	0.134
Triglyceride (mg/dL)	121.9	173	152.40	187.6	**0.026**
HDL (mg/dL)	51	44.3	49.3	35.3	0.758
LDL (mg/dL)	103.3	90.5	116.6	75.6	0.268
ESR (mm/h)	14.96	26.56	47.80	49.0	**<0.001**
Hb (g/dL)	14.08	13.53	12.4	13	0.007
Fibrinogen (mg/dL)	271.59	315.47	374.3	424.0	**<0.001**
Creatinine (mg/dL)	0.90	0.99	1.30	3.0	**<0.001**
BUN (mg/dL)	14.33	19.1	24.3	35.3	**<0.001**

Hemorheologic parameters in different stages of chronic kidney disease

	GFR > 90 mL/min/1.73 m² (N=73)	GFR 60~90 mL/min/1.73 m² (N=19)	GFR 30~60 mL/min/1.73 m² (N=10)	GFR < 30 mL/min/1.73 m² (N=3)	P-value
RBC deformability (EI at 3 Pa, %)	0.320 ± 0.002	**0.314 ± 0.006***	0.313 ± 0.007	0.313 ± 0.012	0.047
Aggregation index (%)	39.76 ± 5.61	**41.94 ± 5.74***	44.38 ± 7.17	46.05 ± 2.67	0.027
Critical shear stress (Pa)	267.97 ± 121.12	298.66 ± 74.20	**411.27 ±199.87§**	344.87 ± 92.66	0.008
Fibrinogen/EI at 3 Pa (mg/dL%)	851.07 ± 196.87	**1034.32 ± 316.59***	**1203.08 ± 245.29§**	**1363.44 ± 273.11†**	<0.001
ESR (mm/h)	14.96 + 14.85	26.58 + 23.72*	47.8 + 21.36§¶	49 + 35.08	<0.001
Fibrinogen (mg/dL)	271.5 ± 57.7	315 ± 103.3	374 ± 69.09§	424 ± 60.6†	<0.001

Data are mean ± SD. Comparison among the groups according to GFR was done using ANOVA and posthoc analysis.
GFR, glomerular filtration rate; RBC, red blood cell; EI, elongation index; ESR, erythrocyte sedimentation rate
P-value represents ANOVA p for the baseline measures among the groups
*P <0.05 between GFR>90 and GFR 60~90, §P < 0.05 between GFR>90 and GFR 30~60, ¶ P < 0.05 between GFR 30~60 and GFR <30, †P < 0.05 between GFR>90 and GFR<30



Hemorheologic parameters at different stages of diabetic nephropathy

	ACR < 30 mg/mmol (N=77)	ACR 30~300 mg/mmol (N=12)	ACR > 300 mg/mmol (N=16)	p-value
AI (%)	39.73 ± 5.51	43.53 ± 6.15	**43.71 ± 6.41¶**	0.010
Critical shear stress (Pa)	266.96 ± 188.24	322.26 ± 66.05	**370.65 ± 173.99¶**	0.008
EI at 3Pa (%)	0.318 ± 0.021	0.308 ± 0.027	0.316 ± 0.02	0.23
Fibrinogen/EI at 3Pa (mg/dL%)	856.01 ± 195.89	**1104.89 ± 381.13***	**1170.65 ± 261.63§**	<0.001

Data are mean ± SD. Comparison among the groups according to GFR was done using ANOVA and posthoc analysis.
P-value represents ANOVA p for the baseline measures among the groups
Abbreviations : ACR, albumin/creatinine ratio; EI, elongation index
*P <0.05 between ACR<30 and ACR 30~300 mg/mmol, §P < 0.05 between ACR 30~300 and ACR>300 mg/mmol,
¶ P < 0.05 between ACR<30 and ACR >300 mg/mmol

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Diabetes (complications & therapy)

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