# Hemorheological approach for early detection of diabetic nephropathy

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# Hemorheological approach for early detection of diabetic nephropathy

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# ABSTRACT

Hemorheological Approach for Early Detection of Diabetic Nephropathy

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**Background:** Hemorheologic alterations or changes in blood viscosity have been suggested to play a role in the pathogenesis of diabetic microvascular complications. We measured various hemorheologic parameters in type 2 diabetes patients at different stages of chronic kidney disease (CKD) and assessed their possible role as early markers of diabetic nephropathy and renal insufficiency.

**Methods:** One hundred-five patients with type 2 diabetes were divided into four groups according to glomerular filtration rate (GFR). Hemorheologic parameters, including erythrocyte deformability, fibrinogen/elongation index (EI), and aggregation index (AI) were measured using microfluidic hemorheometer. Various metabolic parameters were assessed from fasting blood samples and urine albumin/creatinine ratio (ACR) was calculated from first morning voided urine.

**Results**: There were significant differences in RBC deformability, AI, critical stress, fibrinogen/EI, and albumin/creatinine ratio among patients in different stages of CKD (all $p<0.05$), RBC deformability and Fibrinogen/EI significantly differed between normal and CKD 2 patients while there was no such difference in ACR. In multiple regression analysis, Fibrinogen/EI at 3Pa was an independent predictor of GFR (ß=-0.328, $p<0.05$). Also, AI, critical stress, and CSS/EI at 3 Pa, CSS*ESR were significantly different among patients at different stages of diabetic nephropathy, with a significant difference in CSS*ESR between normal and microalbuminuric patients (all $p< 0.05$).

**Conclusions:** CSS*ESR are sensitive parameters measured via point-of-care testing for detecting erythrocyte alterations in early CKD and nephropathy in patients with type 2 diabetes. Further studies are warranted to verify their use as screening tools for diabetic nephropathy and renal impairment.

Key Words : diabetic nephropathy, hemorheololgic parameter, RBC deformability, GFR, Albumin-creatinine ratio

# Hemorheological Approach for Early Detection of Diabetic Nephropathy

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## I. INTRODUCTION

The worldwide pandemic of diabetes and the subsequent complications present major threats to the community health. Diabetic complications consist mainly of vascular diseases, such as microangiopathy and macroangiopathy, and they have been shown to be closely associated with hemorheological abnormalities such as elevated whole blood viscosity[1]. Hemorheological alterations were reported in present in patients with new onset diabetes [1, 2], and other studies suggested that it may precede the development of diabetic microangiopathy[1, 3]. Therefore, hemorheological disturbances seem to occur in the early phase of disease progression[2, 4].

Among factors determining blood viscosity including hematocrit, plasma proteins such as fibrinogen, red blood cell (RBC) deformability, and RBC aggregation[5, 6], previous research was mainly focused on the correlations

between diabetic nephropathy and erythrocyte deformability and aggregation. According to a recent study, all of these factors are intimately connected to one another, and whole blood viscosity is determined not only by these individual factors, but also by their interactions [7]. These changes in whole blood viscosity may in turn play important roles in the pathogenesis of vascular complications associated with diabetes mellitus.

In order to prevent the progression of diabetic complications, an early detection is crucial. Especially, for patients with diabetic nephropathy (DN) treated with optimal therapy at an early phase, the disease can be slowed or prevented from progressing to chronic kidney disease (CKD)[8]. Currently, diabetes patients are encouraged to undergo regular urinary analyses, ultrasonography, and blood examinations to screen for diabetic nephropathy. However, this requires high costs and demands patient compliance, and thus regular checkups for diabetic complications are difficult in clinical settings. Moreover, although an increased excretion of urinary albumin is considered a golden standard for detecting the onset and progression of diabetic nephropathy[9], it has several limitations. Therefore, more simple and reliable biomarkers with higher sensitivity and specificity are needed for early prediction of the onset and monitoring of the progression of DN [10]

In our previous study, there were significant differences in the degree of RBC deformability when comparing diabetes patients with healthy control, and also between diabetes patients with chronic renal disease or end stage renal disease and those with normal renal function[11]. Hemorheologic alterations are assessed by point-of-care testing with 5 μL of whole blood within 30 seconds, and there is a need for discovering a more sensitive marker for early diabetic nephropathy. To our knowledge, the present study is the first study concerning the association between diabetic nephropathy and hemorheology in comparison with the albumin/creatinine ratio (ACR).

In this study, we plan to assess novel markers of hemorheologic disturbances and validate these parameters by comparing with urine albumin creatinine ratio for the early detection of diabetic nephropathy

## II. MATERIALS AND METHODS

### 1 Subjects

One hundred-five type 2 diabetes mellitus patients were enrolled in this study. Diabetes was defined as both previously diagnosed and undiagnosed type 2 diabetes mellitus. Diagnosed diabetes mellitus was based on self-reported responses. The diagnosis of diabetes was based on the following American Diabetes Association criteria: fasting plasma glucose (FPG) ≥126 mg/dL (7.0 mmol/L), or symptoms of diabetes plus casual plasma glucose ≥200 mg/dL (11.1 mmol/L), or 2-h postload glucose ≥200 mg/dL (11.1mmol/L) during a 75-mg oral glucose tolerance test; or glycated hemoglobin (HbA1C) ≥ 6.5% (47.5 mmol/mol).

The subjects were divided into four groups according to their glomerular filtration rate (GFR), calculated using the Modification of Diet in Renal Disease (MDRD) formula as follows: 186 x $(\text{creatinine})^{-1.154}$ x $(\text{age})^{-0.203}$ x (0.742 if female) x (1.210 if black). Seventy-nine subjects were classified as healthy controls (GFR >90 mL/min/1.73 $m^2$ without proteinuria); 19 patients had mild CKD (CKD stage 2: GFR, 60-89 mL/min/1.73 $m^2$); 13 subjects had moderate CKD (stage 3 ~ 5 : GFR < 60 mL/min/1.73 $m^2$).

Women who were pregnant or lactating; and subjects with anemia, acute illness, cancer, abnormal liver function, or other conditions, including any red blood cell disorders, not suitable for study entry according to the researchers' judgment were excluded from the study.

All participants gave the informed consent, and the study was approved by the Institutional Review Board of Gangnam Severance Hospital.

## 2. Design

This study is a cross-sectional study, in which all data and samples were collected at a baseline visit, and includes patients from the Gangnam severance hospital, an 800-bed tertiary care center in Korea. Patient information was obtained from all patients with diabetes by a standardized questionnaire.

## 3. Measurements

### Anthropometric and biochemical measurements

Body weight and height were measured in the morning with light clothing without shoes. Body mass index (BMI) was calculated as body weight in kilograms divided by height in meter squared (kg/m2). Blood pressure was measured twice in the sitting position and a mean value was calculated. Fasting blood samples were drawn and analyzed for HbA1C, serum glucose, cholesterol, triglycerides, HDL and LDL cholesterol, blood urea nitrogen (BUN), creatinine, triglyceride, fibrinogen, hemoglobin (Hb), and the erythrocyte sedimentation rate (ESR). The urine ACR was determined centrally from first voided morning urine in all

patients. Renal function was calculated using the MDRD formula as described above.

## 4. Sample preparation and measurement techniques for hemorheologic parameters

Blood samples were drawn from the antecubital vein into EDTA-containing vacutainers. All analyses were completed within 8 hours of fasting blood collection.

The erythrocyte deformability and aggregation were measured by using a microfluidic hemorheometer (RheoScan-AnD300), RheoMeditech, Seoul, Korea). For deformability measurements, the erythrocyte suspension in high viscous medium (polyvinylpyrrolidone solution) was driven by differential pressure through a microchannel. During the flow, a laser beam (wavelength, 635 nm) from a laser diode of power 1.5 mW passed through the diluted erythrocyte suspension. The diffraction pattern of the flowing erythrocytes at plural shear stresses was projected onto a screen, captured by a charge-coupled device-video camera, and finally analyzed by computer. The elongation index (EI) of the erythrocytes was defined as: $(L - W) / (L + W)$, where L and W are the major and minor axes of the ellipse, respectively. And The elongation index (EI) in RBCs exposed to shear stress (3 Pa) was used to assess deformability.

Critical shear stress (CSS) was measured using native whole blood without adjusting for hematocrit. Critical shear stress was defined as the minimum shear stress required to disperse RBC aggregates. For the CSS measurement, a transient microfluidic technique was adopted with optical detection. When a whole blood sample stored in a reservoir chamber was driven by a pressure differential through a narrow micro-channel (K-01, Rheomeditech, Seoul, Korea), the pressure differential exponentially decreased with time and the flow ceased asymptotically. During the process, the time-varying backscattered light intensity and pressure data were recorded in a computer data file and analyzed. When the backscattered light yielded a maximum, the corresponding time and shear stress were determined as critical time and critical shear stress, respectively. Further details of this technique are provided elsewhere [12].

To assess erythrocyte aggregation, blood samples were perfused to a microchip, and a magnetic rotating mechanism was used to stir the suspension in order to induce shear flow to disaggregate the RBCs. A light signal transmitted through the blood sample was detected by a photodiode, and all data were analyzed by computer .

## 5. Statistical analysis

Statistical analysis was performed using SPSS version 20 (SPSS Inc.,

Chicago, IL, USA). The baseline characteristics are expressed as means ± standard deviations for continuous variables, and frequencies for categorical variables. The statistical significance of differences in categorical variables between groups was tested using the $\chi^2$ test. Statistical differences between the four groups were assessed using one-way ANOVA, with all differences considered significant at $p<0.05$. And we used multiple and logistic regression for show association GFR and orther hemorheologic parameter.

## III. RESULTS

### 1. Baseline characteristics

The participants were divided into 3 groups according to GFR. For comparing the baseline characteristics of the groups, clinical data were obtained and analyzed. There were no significant difference among the groups in terms of sex, systolic blood pressure (SBP), HbA1c, fasting plasma glucose, hemoglobin, fibrinogen, urine ACR, ESR, BMI, total cholesterol, LDL and HDL cholesterol, triglycerides, fibrinogen, BUN, and creatinine. Urine ACR, ESR, Hb, fibrinogen, BUN, and creatinine were significantly different among the groups ($p<0.05$ for all; Table 1)

Table 1. Baseline characteristics of the patients (N=105)

| | GFR > 90 mL/min/1.73 $m^2$ (N=73) | GFR 60~90 mL/min/1.73 $m^2$ (N=19) | GFR < 60 mL/min/1.73 $m^2$ (N=13) | P-value |
|---|---|---|---|---|
| Age, years | 57.8 | 62.5 | 56.6 | 0.124 |
| Sex (female, %) | 41.1 | 47.4 | 50 | 0.856 |
| BMI ($kg/m^2$) | 24.24 | 25.4 | 25.79 | 0.124 |
| Systolic BP (mmHg) | 122 | 123 | 135 | <0.001 |
| Diastolic BP (mmHg) | 73 | 74 | 75.9 | 0.287 |
| HbA1c(%) (mmol/mol) | 7.4 (57) | 9.2 (77) | 8.1 (53) | 0.22 |
| FPG ( mg/dL ) | 149 | 216.95 | 151 | 0.23 |
| Urine ACR (mg/mmol) | 9.86 | 272.63 | 2518.0 | <0.001 |
| T. cholesterol (mg/dL) | 121.99 | 171.16 | 194.46 | 0.338 |
| Triglyceride (mg/dL) | 121.9 | 173 | 160.54 | 0.026 |
| HDL ( mg/dL ) | 51 | 44.3 | 46.08 | 0.758 |
| LDL (mg/dL) | 103.3 | 90.5 | 107.15 | 0.268 |
| ESR (mm/h) | 14.96 | 26.56 | 47.08 | <0.001 |
| Hb (g/dL) | 14.08 | 13.53 | 12.5 | 0.007 |
| Fibrinogen ( mg/dL ) | 271.59 | 315.47 | 385.7 | <0.001 |
| Creatinine ( mg/dL ) | 0.90 | 0.99 | 1.69 | <0.001 |
| BUN ( mg/dL ) | 14.33 | 19.1 | 26.8 | <0.001 |

## 2. Correlations between hemorheologic parameters and GFR

Participants were divided into 3 groups according to their GFR for comparison of the hemorheologic parameters. The elongation index, which indicates the RBC deformability, showed a gradual decrease with the deterioration of GFR (Table 2), and a significant reduction in erythrocyte deformability was observed between the mild CKD group and the healthy controls (0.314 ± 0.006 vs. 0.320 ± 0.002, $p<0.05$; Table 2). The aggregation index, which indicates the RBC aggregation, tended to show an inverse relationship with GFR ($p=0.080$; Table 2), whereas critical shear stress showed a significant difference between CKD(GFR<60) and healthy controls (393.64 vs. 267.97, $p<0.05$; Table 2). CSS/EI at 3 Pa, CSS/EI at Max, CSS*SS 1/2 significantly differed between the moderate CKD groups and the healthy controls ($p<0.05$; Table 2). Furthermore, CSS*ESR was found to significantly differ between the moderate CKD and mild CKD groups, as well as between the mild CKD and the healthy control groups ($p<0.05$ for all). In multiple regression analysis, CSS*ESR was an independent predictor of GFR in a model adjusted with BMI, Hb, ESR , and age(ß = -0.328 , $p < 0.05$).

Table 2. Hemorheologic parameters in different stages of chronic kidney disease.

| | GFR < 60 mL/min/1.73 $m^2$ (N=13) | GFR 60~90 mL/min/1.73 $m^2$ (N=19) | GFR > 90 mL/min/1.73 $m^2$ (N=73) | P-value |
|---|---|---|---|---|
| RBC deformability (EI at 3 Pa) | 0.313 ± 0.020 | 0.314 ± 0.006* | 0.320 ± 0.002 | 0.047 |
| Aggregation index | 44.77 ± 6.34 | 41.94 ± 5.74 | 39.76 ± 5.61 | 0.027 |
| Critical stress | 393.64 ± 180.31 | 298.66 ± 74.20 | 267.97 ± 121.12 | 0.008 |
| CSS*ESR | 21345.13 ± 4878.54§ | 8585.34 ± 2091.24* | 4655.42 ± 720.87 | <0.001 |
| CSS/EI at 3 Pa | 1289.16±683.03§ | 987.98 ± 264.68 | 845.73 ± 405.93 | 0.003 |
| CSS/EI Max | 695.29 ± 86.78§ | 530.89 ± 134.36 | 477.48 ± 213.49 | 0.05 |
| CSS*SS1/2 | 1001.67 ± 628.83§ | 752.50 ± 248.39 | 619.31 ± 330.55 | 0.03 |
| ESR | 48.08 ± 23.34§ | 26.58 ± 23.72* | 14.96 ± 14.85 | <0.001 |
| Fibrinogen | 374 ± 69.09§ | 315 ± 103.3 | 271.5 ± 57.7 | <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; SS1/2, Shear stress 1/2

*P <0.05 between GFR>90 and GFR 60~90

§P < 0.05 between GFR>90 and GFR <60

## 3. Factors assoacited with hemorheologic parameters

Fibrinogen, which affects the aggregation index, also showed significant inverse correlations with GFR ($p<0.05$, Table 1). Fibrinogens and AI showed similar tendencies, with fibrinogen significantly differing between

moderate CKD patients and healthy controls. Moreover, critical shear stress tended to increase with the rate of fibrinogen, and it showed a similar tendency to the aggregation index, with a significant difference observed between moderate CKD and healthy controls (411.27 vs. 267.97, $p<0.05$, Table 1). In addition, RBC deformability, namely the elongation index at 3 Pa, was compared among patients in tertiles according to HbA1c level (HbA1c ≤ 7.0% vs. 7.0 < HbA1c ≤ 9.0% vs. HbA1c > 9.0%). RBC deformability decreased gradually in the order of increasing HbA1c (0.324 ± 0.014 vs. 0.317 ± 0.021 vs. 0.304 ± 0.021, respectively, $p < 0.001$). This finding is consistent with the well-known concept of decreased RBC deformability in hyperglycemic condition.

## 4. Correlations between urinary albumin creatinine ratio and hemorheologic parameters

ACR showed a significant inverse correlation with GFR ($p<0.05$). ACR differed significantly between the moderate CKD group and healthy controls ($p <0.05$), but not between the mild CKD group and healthy controls (Figure 1). Significant correlations were observed between various hemorrhologic parameters including AI, Critical stress, CSS/EI at 3Pa, CSS/EI at Max, CSS*SS1/2, CSS*ESR, ESR and urine ACR ($r^2$ = 0.452, 0.285, 0.253, 0.248, 0.255, 0.321 and 0.246; $P < 0.001$, 0.009,

0.009, 0.011, 0.01, 0.001 and 0.05, all respectively,). Serum fibrinogen was also in a positive correlation with urine ACR ($r^2 = 0.426$, $P < 0.001$). When subjects were divided into normal, microalbuminuria, and macroalbuminuria groups according to ACR, there wase significant differences in Fibrinogen/EI at 3 Pa between normal and microalbumiria group (Table 3, P=0.003).

Table 3. Hemorheologic parameters in 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 | 99.73 ± 5.51 | 43.53 ± 6.15 | 43.71 ± 6.41¶ | 0.01 |
| Critical stress | 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 |
| CSS * ESR | 856.01 ± 195.89 | 1104.89 ± 381.13* | 1170.65 ± 261.63§¶ | <0.001 |
| CSS/EI at 3 Pa | 4243.18 ± 685.96 | 12658.81 ± 3401.64 | 17420.23 ± 4181¶ | 0.006 |
| CSS/EI at max | 475.31 ± 208.43 | 576.05 ± 119.41 | 654.41 ± 302.91¶ | 0.008 |
| CSS*SS 1/2 | 623.32 ± 327.33 | 788.23 ± 230.25 | 942.18 ± 590.06¶ | 0.006 |
| ESR | 14.7 ± 1.65 | 37.75 ± 8.54* | 39.81 ± 5.62 | <0.001 |

Data are mean ± SD. Comparison among the groups according to GFR was done using ANOVA and posthoc analysis.

Abbreviations : ACR, albumin/creatinine ratio; EI, elongation index

*P <0.05 between ACR>30 and ACR 30~300

§P < 0.05 between ACR 30~300 and ACR>300

¶ P < 0.05 between ACR<30 and ACR >300

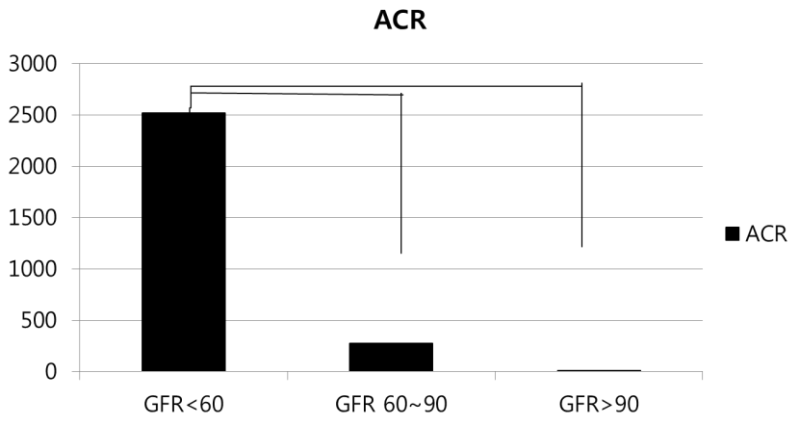


Figure 1. Urine albumin/creatinine ratio (ACR) in different stages of CKD. ACR differed significantly between CKD 3 group and healthy controls, but no such difference was observed between the CKD 2 group and healthy controls.

*P-value < 0.05

A: GFR <60 mL/min/1.73 $m^2$

B: GFR 60~90 mL/min/1.73 $m^2$

D: GFR > 90 mL/min/1.73 $m^2$

GFR, glomerular filtration rate

## IV. DISCUSSION

In present study, we demonstrated significant differences in several hemorheologic parameters in different stages of CKD and diabetic nephropathy in patients with type 2 diabetes, and it was valid in differentiating patients with mild CKD from normal renal function as well as microalbuminuria from normal. Hemorheologic alterations showed close linear relationships to urinary albumin creatinine ratio.

More than 50 years have passed since Skovborg et al. first studied blood viscosity in diabetic patients [13]. Since then, many researchers have reported that blood viscosity is significantly increased in diabetic patients, and there have been numerous studies on the correlations between erythrocyte deformability and diabetic microangiopathies. For example, Brown et al. reported an association between reduced erythrocyte deformability and diabetic nephropathy [14]. They demonstrated greater impairment of erythrocyte deformability in patients with diabetes with normal renal function compared with non-diabetic controls. Subsequently, more severe impairment in erythrocyte deformability was noted in patients with diabetic nephropathy.

Elevated blood viscosity in patients with diabetes can be explained by an increase in erythrocyte aggregation and a decrease in erythrocyte deformability. Hyper-aggregation of erythrocytes increases low-shear viscosity, whereas decreased cell deformability increases high-shear

viscosity. Generally, hyperglycemia leads to membrane glycation, which stiffens the erythrocyte membranes. In turn, the stiffened membranes reduce cellular deformability, which is frequently observed in local hypoxia and microangiopathies, potentially resulting in the development of diabetic nephropathy .

Currently, diabetic nephropathy is divided into subgroups according to the urine ACR, and the progression of DN is estimated by urinary analysis (ACR and protein/creatinine ratio), blood sampling (GFR, creatinine), and renal sonography. In the early, microalbuminuria stage, the progression of nephropathy can be reversed if the proper management is started in time, emphasizing the importance of early detection and diagnosis of this disorder.

However, there is currently no tool allowing easy, point-or-care testing for the early diagnosis for DN. Moreover, the degree of albuminuria is not necessarily linked to disease progression in patients with diabetic nephropathy secondary to either type 1 or type 2 diabetes [15]. This was illustrated in a report of 79 patients with type 1 diabetes from the Joslin Kidney Study, who were followed for a mean of 12 years after the onset of moderately increased albuminuria [9]. Twenty-three of the patients progressed to advanced disease (GFR <60 mL/min). Among these patients, 11 had either stable moderately increased albuminuria or regression to

normal albuminuria. Presently, the factor(s) responsible for progressive GFR decline in nonalbuminuric diabetic nephropathy are not known. Therefore, there is a need for a new marker that can detect microalbuminuria as well as early renal impairment.

In our study, the patients were classified according to their GFR, which represents the actual renal function. The GFR, which is the volume of fluid filtered from the renal glomerular capillaries into the Bowman's capsule per unit time, is clinically important because it represents an accurate measurement of renal function [11]. Moreover, blood urea nitrogen and creatinine are not raised above the normal range until 60% of total kidney function is lost.

Our study results showed that renal function was associated with not only RBC deformability, aggregation index, and critical stress, but also with ESR and fibrinogen. ESR is known to be frequently elevated in patients with renal insufficiency, and accordingly, we found that the elevation of ESR was higher when the renal insufficiency was more severe. Fibrinogen has been previously demonstrated to be associated with coronary artery disease and nephropathy in patients with diabetes, which was confirmed by our results.

A significant reduction in the erythrocyte deformability was observed between the mild CKD group and non CKD controls (EI at 3 Pa: 0.314 ±

0.006 vs. 0.320 ± 0.002 $p<0.05$). Furthermore, the CSS*ESR significantly differed between the moderate and mild CKD groups, and between the mild CKD group and healthy controls ($p<0.05$), suggesting that erythrocyte deformability and CSS*ESR could potentially be used clinically for identifying patients at risk of developing renal impairement.

In terms of urine ACR, we found a negative correlation with GFR, and a significant difference was observed between the moderate CKD and healthy control groups (P value <0.05), but not between the mild CKD group and healthy controls. Moreover, when subjects were divided according to ACR, there was a significant difference in CSS*ESR between normal and microalbumirnuria group, which suggests its role in detecting nearly diabetic nephropathy. This is in accordance with a previous study, which was conducted on smaller number of patients.

Patients with diabetes are required to undergo regular checkups, including urinary and blood analyses and ultrasonography, to detect potential complications. However, this requires high patient compliance and is associated with high costs to the patients. Thus, regular checkups for diabetic microcomplications are difficult in a clinical setting. If we can develop accurate clinical hemorheologic markers, it would be possible to detect early deterioration of renal function and diabetic nephropathy using only 5 μL blood within 30 seconds, which would result in increased

compliance and enable more patients to detect their diabetic complications earlier.

The present study has a number of limitations. First, it is a relatively small study with only 105 participants; further large-scale studies are hence needed on the topic before any firm conclusions can be drawn. With a larger patient sample, the exact tendencies of the hemorheologic factors in the groups can be analyzed, hopefully resulting in the identification of parameters that will enable us to estimate nephropathy. Nevertheless, a major strength of the present study is that this is the first study on the association of diabetic nephropathy and hemorheology in comparison with ACR.

In summary, examination of hemorheological factors was superior or at least comparable to ACR in terms of its simplicity in measurement and early detection of renal impairment and diabetic nephropathy in type 2 diabetes patients. 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

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ABSTRACT (IN KOREAN)

# 당뇨신병증의 조기 발견을 위한 혈유변학적 접근

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이 서 희

배경: 당뇨 환자의 경우 적혈구 변형능, 적혈구 응집성과 같은 혈유변학적 인자의 변화가 생기게 되며, 이러한 변화는 전혈의 점성을 증가시키며 당뇨병의 미세혈관 합병증의 병인에 있어서 중요한 역할을 할 가능성이 제기되고 있다. 따라서 이러한 혈유변학적 인자들을 당뇨환자에서 측정하여, 당뇨 신병증 및 신기능 저하와의 관련성을 조사하였다.

방법: 105명의 제 2형 당뇨병 환자를 대상으로 사구체 여과율에 따라서 4 그룹으로 나누어 연구를 진행하였다. 적혈구 변형능, 적혈구응집성을 포함한 혈유변학적 인자들을 측정하였고, 소변 알부민/크레아티닌 비율 및 사구체여과율 저하와의 관련성을 살펴보았다.

결과: 당뇨신병증의 단계와 적혈구 변형능, 응집성, 임계 전단 응력, 섬유소원의 유의미한 차이가 있었다(all $p<0.05$). 그 중 적혈구 변형능과 Fibrinogen/EI at 3 Pa는 정상군과 만성신부전 2 단계에서 유의미한 차이를 보였지만, 알부민/크레아티닌 비율에 따라서는 차이가 없었다. 또한 다중회귀분석에서 Fibrinogen/EI at 3 Pa 은 사구체여과율을 예측하는데 있어서 독립적인 인자로써 보여졌다(ß=-0.328, $p<0.05$).

결론: 적혈구 변형능과 Fibrinogen/EI at 3Pa는 만성신부전의

초기 단계를 진단하는데 있어서 유용한 지표로 쓰일 수 있다. 이러한 혈유변학적 인자들을 이용한다면 당뇨 신병증을 당뇨 미세혈관 합병증의 조기진단에 큰 도움이 될 수 있을 것이다.

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핵심되는 말 : 당뇨신병증, 혈유변학적 인자, 적혈구 변형능, 사구체여과율, 알부민/크레아티닌 비율