

Association Between Urinary Albumin Excretion and Serum Dehydroepiandrosterone Sulfate Concentrations in Women With Type 2 Diabetes

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Both elevated urinary albumin excretion (UAE) and low serum concentrations of dehydroepiandrosterone (DHEA) have been linked with increased cardiovascular disease (CVD) mortality in men (1–5). We have recently demonstrated that serum DHEA sulfate (DHEA-S) concentrations correlated inversely with degree of UAE in men with type 2 diabetes (6). However, findings supporting a protective role of DHEA for CVD have been inconsistent in women (7–9). Furthermore, to our knowledge, the relationship between serum DHEA-S concentrations and degree of UAE, a marker of CVD, has never been explored in women with type 2 diabetes. We therefore investigated the relationship between serum DHEA-S concentrations and degree of UAE, as well as pulse wave velocity (PWV), a marker of arterial stiffness, in women with type 2 diabetes.

RESEARCH DESIGN AND METHODS

— Relationships of UAE to serum DHEA-S concentrations and to major cardiovascular risk factors were investigated in 254 consecutive women with type 2 diabetes who were recruited from the outpatient clinic at the Kyoto

Prefectural University of Medicine. Most patients were postmenopausal women ($n = 244$), and no patients received hormone replacement therapy. Mean values for BMI, blood pressure, and biochemical parameters obtained during the preceding year were used for statistical analysis. Patients enrolled in this study were almost stable for control of diabetes, hypertension, and dyslipidemia, and there were few changes to their medications during the preceding year. Moreover, the relationship of serum DHEA-S concentrations to PWV was investigated in a subgroup of patients ($n = 153$). Serum DHEA-S concentrations (normal range 50–1,950 ng/ml) was measured by the Coat-A-Count DHEA-S kit (Diagnostic Products, Los Angeles, CA). Urinary albumin and creatinine concentration were determined in an early morning spot urine. UAE was measured with an immunoturbidimetric assay. A mean value for urinary albumin excretion was determined from three urine collections. Brachial-ankle PWV was measured using a Colin Waveform analyzer (form PWV/ABI; Colin Medical Technology, Komaki, Japan) (10). Nephropathy was graded as follows: normoalbuminuria, UAE <30

mg/g creatinine; microalbuminuria, UAE 30–300 mg/g creatinine; or macroalbuminuria, UAE >300 mg/g creatinine. Patients were excluded if they were taking any medications likely to affect serum DHEA-S concentrations. Approval for the study was obtained from the local research ethics committee, and informed consent was obtained from all participants. ANOVA were conducted to assess statistical significance of differences between groups using Stat View software (version 5.0; SAS Institute, Cary, NC). Because UAE showed a highly skewed distribution, logarithmic (log) transformation of these values was carried out before performing correlation and regression analysis. The relationships between serum DHEA-S concentrations and logUAE or PWV were examined by Pearson's correlation analyses. To examine the effects of various factors on logUAE, the following factors were considered as independent variables for multiple regression analysis: serum DHEA-S concentration, age, duration of diabetes, BMI, A1C, systolic blood pressure, diastolic blood pressure, and plasma total cholesterol, triglyceride, and HDL cholesterol concentrations. All continuous variables are presented as means \pm SD. A P value <0.05 was considered statistically significant.

RESULTS — Clinical characteristics of the 254 female patients with type 2 diabetes enrolled in this study are as follows: mean age, duration of diabetes, BMI, A1C, systolic blood pressure, diastolic blood pressure, and plasma total cholesterol, triglyceride, HDL cholesterol, and serum DHEA-S concentration were 66.0 ± 10.9 years, 14.5 ± 10.3 years, 22.8 ± 3.5 kg/m², $7.5 \pm 1.2\%$, 131 ± 17 mmHg, 72 ± 10 mmHg, 5.33 ± 0.83 mmol/l, 1.38 ± 0.85 mmol/l, 1.53 ± 0.44 mmol/l, and 718 ± 477 ng/ml, respectively. Serum DHEA-S concentrations in patients with normoalbuminuria ($n = 148$), microalbuminuria ($n = 78$), and macroalbuminuria ($n = 28$) were $779 \pm$

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Abbreviations: CVD, cardiovascular disease; DHEA, dehydroepiandrosterone; DHEA-S, DHEA sulfate; PWV, pulse wave velocity; UAE, urinary albumin excretion.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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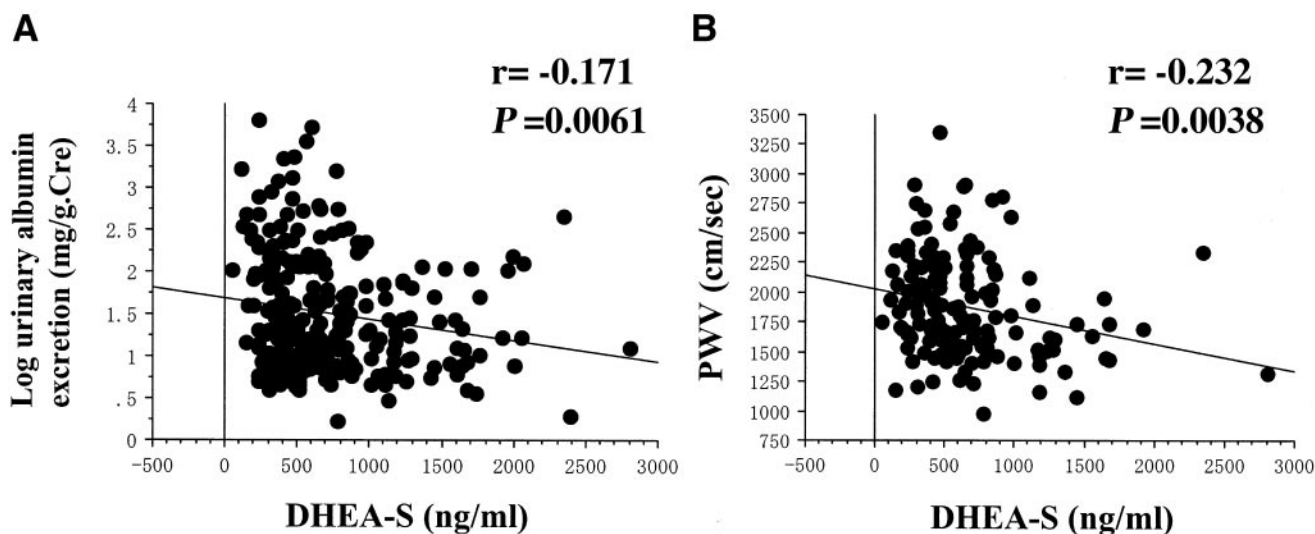


Figure 1—Correlation between serum DHEA-S concentrations and logUAE (A) and between serum DHEA-S concentrations and PWV (B) in women with type 2 diabetes.

487 ng/ml, 681 ± 455 ng/ml, and 499 ± 421 ng/ml, respectively. Serum DHEA-S concentrations were lower in patients with macroalbuminuria than those with normoalbuminuria ($P = 0.0041$). Inverse correlation was found between serum DHEA-S concentrations and logUAE ($r = -0.171$, $P = 0.0061$) (Fig. 1A), which is applicable to patients with menopause ($r = -0.147$, $P = 0.0216$). Age ($r = 0.261$, $P < 0.0001$), duration of diabetes ($r = 0.218$, $P = 0.0010$), BMI ($r = 0.233$, $P = 0.0005$), A1C ($r = 0.179$, $P = 0.0023$), systolic blood pressure ($r = 0.347$, $P < 0.0001$), and plasma triglyceride concentrations ($r = 0.135$, $P = 0.0374$) were positively associated with logUAE, whereas plasma HDL cholesterol concentration ($r = -0.154$, $P = 0.0174$) was inversely associated with logUAE. Multiple regression analysis demonstrated that duration of diabetes ($\beta = 0.191$, $P = 0.0057$), BMI ($\beta = 0.161$, $P = 0.0162$), systolic blood pressure ($\beta = 0.279$, $P = 0.0007$), and serum DHEA-S concentrations ($\beta = -0.160$, $P = 0.0182$) were independent determinants of logUAE. Serum DHEA-S concentrations correlated inversely with PWV ($r = -0.232$, $P = 0.0038$) (Fig. 1B), which is applicable to patients with menopause ($r = -0.215$, $P = 0.0074$).

CONCLUSIONS— The present study found inverse associations between serum DHEA-S concentrations and degree of UAE and between serum DHEA-S concentrations and PWV. Low serum concentrations of DHEA-S are associated with decreased

insulin sensitivity, decreased HDL cholesterol, increased platelet aggregation (11–14), endothelial dysfunction, and low-grade chronic inflammation (15,16); these factors are associated with both elevated UAE and higher CVD mortality (17–20). The inverse association between serum DHEA-S concentrations and degree of UAE might be partially explained by the positive association between degree of UAE and duration of diabetes because Parker et al. (21) previously demonstrated that low serum DHEA concentration is a marker of chronic disease. To our knowledge, this is the first study that has examined the relationship between serum DHEA-S concentrations and degree of UAE in women with type 2 diabetes. However, the cross-sectional nature of our study does not permit determination of causality. Large prospective trials and interventional studies are needed to better assess the relationship between serum DHEA-S concentrations and degree of UAE in women with type 2 diabetes.

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