

## Factors associated with serum total homocysteine level in type 2 diabetes

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Received: 21 June 2007 / Accepted: 18 December 2007 / Published online: 29 March 2008  
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### Abstract

**Objectives** The aim of this study was to investigate the determinants of serum total homocysteine level (tHcy) in patients with type 2 diabetes mellitus (DM) according to sex. **Methods** A total of 1,276 Japanese, diabetics ( $n = 280$ ) with a control group of non-diabetics ( $n = 996$ ), were enrolled into the study from 2003 to 2005. This cross-sectional study was conducted for all the subjects, using personal data regarding clinical characteristics and lifestyle. Multiple regression analysis was performed to analyze the association of tHcy with selected factors. **Results** In diabetic subjects, estimated glomerular filtration rate (eGFR) and serum creatinine levels (Cre), even those within the normal range, were strongly associated with tHcy after adjustment in both sexes; the standardized partial regression coefficient of eGFR for tHcy was  $-0.251$ , ( $p = 0.001$ ) in diabetic men and  $-0.523$ , ( $p < 0.001$ ) in diabetic women. Furthermore, the eGFR of the diabetics, except patients with nephropathy, also had significant association with tHcy in both sexes. Fasting plasma glucose levels and serum triglyceride levels were

strongly associated with tHcy in diabetic men only. HbA1c was also associated with tHcy in diabetic men only, though not as significantly. Age and presence of hypertension were significantly associated with tHcy in women.

**Conclusions** This study suggests that there are some differences in the factors associated with tHcy between diabetics and non-diabetics, and between the sexes. There is, therefore, circumstantial evidence that elevated tHcy should be evaluated clinically. Because tHcy was strongly associated with eGFR and Cre, even within the normal ranges, tHcy may have important implications regarding the microangiopathy of the kidney and atherosclerosis.

**Keywords** Homocysteine · Type 2 diabetes mellitus · Lifestyle · Estimated glomerular filtration rate · Serum creatinine

### Introduction

Homocysteine is a sulfur-containing amino acid formed during metabolism of the essential amino acid methionine [1, 2]. Serum total homocysteine concentration (tHcy) has been recognized as an atherogenic factor, promoting oxidative stress, inflammation, thrombosis, endothelial dysfunction, and cell proliferation [2–4]. In addition, many previous epidemiologic studies suggest that elevated tHcy is a new, strong, and independent risk factor of coronary heart disease (CHD) and stroke [5–7]. Also in Japan, several previous studies reported that tHcy was an independent risk factor of ischemic stroke [8, 9].

It has also been reported that several factors, including age, gender, smoking, alcohol consumption, malignancies, thyroid disease, renal failure, nutrition (deficiency of folic acid, Vitamin B6 and B12), medication, and gene type of

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