

Hyperhomocysteinaemia predicts the decline in pulmonary function in healthy male smokers

K. Nunomiya^{*}, Y. Shibata^{*}, S. Abe^{*}, S. Inoue^{*}, A. Igarashi^{*}, K. Yamauchi^{*}, Y. Aida^{*}, H. Kishi^{*}, M. Sato^{*}, T. Watanabe^{*}, T. Konta^{*}, Y. Ueno[#], T. Kato[#], H. Yamashita[#], T. Kayama[#] and I. Kubota^{*}

^{*}*Department of Cardiology, Pulmonology, and Nephrology, #Global Center of Excellence Program Study Group, Yamagata University School of Medicine, Yamagata, Japan*

Online Data Supplements

RESULTS

Table S1. Univariate regression analysis of factors that were predictive for plasma homocysteine levels

Univariate

Variable	Coefficient	SE	p value
Age	0.087	0.009	<.0001
Male gender	1.291	0.092	<.0001
BMI	0.020	0.029	0.503
Brinkman index	0.002	0.000	<.0001
mean BP	0.056	0.009	<.0001
HbA _{1c}	-0.018	0.138	0.897
ALT	0.022	0.007	0.001
sCr	7.127	0.412	<.0001
TG	0.007	0.001	<.0001
TC	-0.021	0.003	<.0001
%FVC	-0.032	0.007	<.0001
%FEV ₁	-0.030	0.006	<.0001

BMI: body mass index; BP: blood pressure; HbA_{1c}: haemoglobin A_{1c}; ALT:

alanine aminotransferase; sCr: serum creatinine; TG: triglyceride; TC: total

cholesterol; %FVC: percent predicted forced vital capacity; %FEV₁: percent

predicted forced expiratory volume in 1 s

Table S2. Differences in pulmonary function parameters between subjects with homocysteine levels above or below the cut-off value

	Hcy $\leq 11 \mu\text{M}$ ($n = 62$)	Hcy $> 11 \mu\text{M}$ ($n = 81$)	p value
%FVC _{first}	100.28 \pm 13.61	95.96 \pm 14.63	0.073
%FVC _{second}	105.12 \pm 14.43	99.54 \pm 15.24	0.028*
%FEV ₁ _{first}	98.66 \pm 14.20	94.64 \pm 18.30	0.155
%FEV ₁ _{second}	95.57 \pm 14.54	92.83 \pm 19.82	0.026*
FEV ₁ /FVC _{first} (%)	77.25 \pm 6.75	76.96 \pm 9.52	0.837
FEV ₁ /FVC _{second} (%)	73.86 \pm 7.96	72.02 \pm 10.24	0.244
Δ FEV ₁ /year (%)	-0.83 (-1.57, 0.37)	-1.77 (-2.84, 0)	0.006*

Hcy data was not available for four of the 147 subjects. Differences in Δ FEV₁/year (%) between subjects with Hcy $\leq 11 \mu\text{M}$ and those with Hcy $> 11 \mu\text{M}$ were evaluated by the Mann-Whitney U test, because the data was not normally distributed. Differences in all other variables were evaluated by Student's t test. "first" indicates spirometry data at the first visit and "second" indicates spirometry data at the second visit. Hcy: homocysteine; FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 s; Δ FEV₁/year (%): percent annual decline in FEV₁

FIGURE LEGENDS

FIGURE S1. Distribution of percent annual decline in FVC and FEV₁. The distributions of percent annual decline in FVC [dFVC/Y (%)] (A) and FEV₁ [dFEV₁/Y (%)] (B) are shown as histograms. Dashed lines indicate the limit of the first quintile of percent annual decline in the spirometric measurements. FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 s

FIGURE S2. Determination of the cut-off value of plasma homocysteine (Hcy) for discriminating subjects who showed a decline in FEV₁. Receiver operating characteristic (ROC) curve analysis was performed to determine the cut-off value of Hcy for discriminating the subjects who showed a decline in FEV₁. The area under the curve (AUC) was 0.701, and the cut-off value was 11.1 μM, with a sensitivity of 0.897 and a specificity of 0.518. FEV₁: forced expiratory volume in 1 s