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Is homoarginine level associated with high cardiovascular risk and mortality?

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Arginine is used by several nitric oxide syntazes as substrate for nitric oxide production, thus influencing endothelial function. Even though little data is available, there may be a relation between homoarginine and cardiovascular risk

Taking in consideration this fact, the level of homoarginine was determined in over 3000 patients referred to coronary angiography enrolled in LURIC (The Ludwigshafen Risk and Cardiovascular Health study)- a prospective study of individuals in whom the cardiovascular and metabolic phenotypes CAD, MI, dyslipidaemia, hypertension, metabolic syndrome and diabetes mellitus have been defined or ruled out using standardized methodologies in all study participants with the aim of identification and assessment of environmental and genetic factors for atherosclerosis and related metabolic diseases, and in over 1000 type 2 diabetes mellitus patients receiving maintenances hemodialysis enrolled in 4D study (Die Deutsche Diabetes Dialyse Studie) – a prospective, randomized, double-blind study involving 178 dialysis centers throughout Germany whose aim is to provide important information on the efficacy and safety of atorvastatin to support its use in patients with an impaired renal function who are at a high risk of vascular morbidity and mortality.

The median follow up was 7.7 years for LURIC patients and 4 years for 4D patients, during follow up 766 patients (23.2%) died in LURIC group and 608 (48.4%) in 4D group so hemodialysed patients had a 5-fold increased mortality rate compared with LURIC patients. The mean homoarginine level was 1.2±0.5 μmol/l in 4D study versus 2.6±1.1 μmol/l in LURIC study. A >4-fold higher rate of dying of cardiovascular disease (hazard ratio 4.1, 95% confidence interval 3.0 to 5.7) was determined for patients in the lowest quartile(<1.85 μmol/L) than patients in the highest quartile (>3.1 μmol/L).Mortality which was 2-fold higher in 4D study patients in the lowest quartile (<0.87 μmol/L) than in patients in the highest quartile (>1.4 μmol/L).

Being known that homoarginine is excreted by the kidney, the results are somehow controversial, higher levels of homoarginine being expected in patients with impaired renal failure. An possible explanation is the fact that the kidney is the place where L lysine is transaminidated to homoarginine. But more studies are necessary to elucidate the mechanisms involved, eventually in asymptomatic individuals. ❑

Comment on a paper:

W März, A Meinitzer, C Drechsler et al – Homoarginine, Cardiovascular Risk, and Mortality. *Circulation* 2010; 122:967-975