Institutionen för klinisk vetenskap, intervention och teknik (CLINTEC) Enheterna för Baxter Novum och Medicinska Njursjukdomar

DETERMINANTS AND CLINICAL IMPLICATIONS OF CIRCULATING FATTY ACIDS IN INDIVIDUALS WITH CHRONIC KIDNEY DISEASE

av **Xiaoyan Huang** *M.D.*

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i föreläsningssalen, plan 4, Novum, Hälsovägen 7, Flemingsberg, Stockholm,

Onsdagen den 29 maj 2013, kl 09.30



Huvudhandledare: Docent Juan Jesús Carrero MMK, Karolinska Institutet

Bihandledare: Adj. Prof. Bengt Lindholm CLINTEC, Karolinska Institutet

Prof. Peter Stenvinkel CLINTEC, Karolinska Institutet

Dr. Abdul Rashid Qureshi CLINTEC, Karolinska Institutet Fakultetsopponent:
Docent Ola Samuelsson
Njurmedicin, Institutionen för
intermedicin, Sahlgrenska
universitetssjukhuset, Göteborg

Betygsnämnd:

Docent Naomi Clyne, Avdelningen för Njurmedicin, Institutionen för Kliniska Vetenskaper, Lund, Lunds Universitet

Docent Mats Gåfvels Institutionen för laboratoriemedicin, Lunds universitet, Lund

Adj. Prof. Mats Eriksson Institutionen för medicin, Huddinge Karolinska Institutet

Stockholm 2013

Abstract

Determinants and clinical implications of circulating fatty acids in individuals with chronic kidney disease

Xiaoyan Huang
Divisions of Baxter Novum and Renal Medicine, CLINTEC
Karolinska Institutet, Stockholm, Sweden

Patients with chronic kidney disease (CKD) have a high risk of cardiovascular morbidity and mortality. Adding to traditional risk factors, e.g., Framingham risk factors, novel risk factors including inflammation, insulin resistance (IR) and metabolic syndrome (MetS) are being detected in patients with advanced CKD. Previous research demonstrates a promising possibility of improving patient outcomes by dietary manipulation, which could be an essential part of multifaceted interventions. This thesis tries to increase our understanding of circulating fatty acids as a reflection of dietary intake in patients with CKD, with special emphasis on their clinical determinants and outcome implications.

Study 1 identifies fatty acids in serum cholesterol esters and adipose tissue that are adequate biomarkers of habitual intake in CKD. We found that linoleic acid (LA), eicosapentaenoic acid, docosahexaenoic acid, and palmitic acid in serum cholesterol esters and adipose tissue are good indicators of the habitual dietary fat intake in elderly men with CKD. Dietary fish intake reflects well the intake of *n*-3 polyunsaturated fatty acids (PUFA) of marine origin.

Study 2 investigates the implications of circulating essential PUFA, as a reflection of long-term dietary intake, on the inflammatory risk profile and clinical outcome of dialysis patients. LA in plasma phospholipids is inversely associated with interleukin-6 and all-cause mortality in dialysis patients. Associations between n-3 PUFA, inflammation and mortality were not observed.

Study 3 investigates clinical determinants and outcome implications of estimated stearoyl-CoA desaturase-1 (SCD-1) activities of the liver and adipose tissue, as indicators of saturated fat intake, in dialysis patients. We found that both hepatic and adipose tissue SCD-1 activity indices independently relate with interleukin-6 and predict mortality in dialysis patients.

Study 4 assesses cross-sectional relationships between serum fatty acid patterns, MetS, IR and inflammation in CKD. A serum fatty acid pattern reflecting low LA and high saturated fatty acids strongly associates with MetS, IR and C-reactive protein, while another pattern reflecting high *n*-3 PUFA is not linked with these risk factors, in two independent cohorts of elderly individuals with CKD.