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ABSTRACTS

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Th-W53:6 THE EFFECT OF N-3 FATTY ACIDS ON HEART RATE VARIABILITY IN PATIENTS TREATED WITH CHRONIC HEMODIALYSIS

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Objectives: Patients with chronic renal failure (CRF) have an increased mortality, mainly due to cardiovascular disease (CVD). Depressed heart rate variability (HRV) is a predictor of mortality in patients with CVD. Previous studies have shown that supplementation with n-3 polyunsaturated fatty acids (PUFA) may increase HRV and protect against sudden cardiac death. The aim of the present study was to address the effect of n-3 PUFA on HRV in patients treated with chronic hemodialysis (HD).

Methods: Patients with documented CVD, treated with chronic HD for at least 6 months were randomised to treatment with n-3 PUFA or control treatment (olive oil). At baseline and after three months, patients were evaluated with 24-hour HRV measurement and blood-samples, to assess the content of n-3 PUFA in plasma phospholipids.

Results: Thirty patients were included. The two groups were comparable regarding baseline characteristics and HRV. After supplementation with n-3 PUFA for three months there was a significant decrease in heart rate (HR) from 73.4 bpm to 70.5 bpm and a corresponding increase in the RR interval. When the two groups were compared, this did not remain significant. n-3 PUFA did not significantly affect other HRV parameters.

Conclusion: Supplementation with n-3 PUFA for three months did not significantly increase HRV. However, in the n-3 PUFA group there was a reduction in HR of 2.9 bpm, results that may be of clinical interest.

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Th-W53:7 EFFECT OF OMEGA-3 PUFA ON CAROTID IMT AND HAEMOSTASIS IN HYPERTRIGLYCERIDEMIC PATIENTS: A LONGITUDINAL PILOT STUDY IN PRIMARY PREVENTION

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Objective: To measure carotid intima-media thickness (C-IMT), IMT texture, lipids, platelet function and haemostatic variables during omega-3 polyunsaturated fatty acids (PUFA) treatment.

Methods: 64 hypertriglyceridemic patients were administered omega-3 PUFA or placebo for 2 years. C-IMT and IMT texture were assessed by B-mode ultrasound. Lipids, platelet function and haemostatic variables were determined by validated methods.

Results: Compliance to the treatment was documented by plasma fatty acid composition. During treatment a fall of triglyceride levels, concomitant to a rise of HDL-C and LDL-C level, was observed in the group on active treatment. Platelet function, but not FVIIc and fibrinogen levels, was significantly reduced by omega-3 PUFA. Over 2 years, C-IMT increased significantly with respect to baseline in placebo but not in the treated group. In addition, C-IMT texture was significantly affected by omega-3 PUFA. Treatment effect, however, did not reach the statistical significance neither in terms of IMT changes nor in terms of IMT texture.

Conclusion: Our results are suggestive of a beneficial effect of omega-3 PUFA on IMT progression and IMT texture that deserve to be more deeply investigated in a larger sample of patients. Nevertheless the pilot nature of this study, the beneficial effect of omega-3 PUFA on platelet function, triglycerides and HDL-C is clearly highlighted.

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Th-W54 LIPOPROTEIN PARTICLE**Th-W54:1 RECENT ADVANCES IN THE STUDY OF THE SMALL DENSE LOW-DENSITY LIPOPROTEIN PARTICLE PHENOTYPE**

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Objective: Small dense LDL particles are being increasingly recognized as an important risk factor for coronary heart disease (CHD). The objective of this presentation is to provide an overview of the latest research developments in that area.

Methods: Results were retrieved through literature search in PUBMED, with emphasis on data from our own group.

Results: Compelling evidence from epidemiological, clinical and *in vitro* studies associate small dense LDL to an increased risk of CHD [1]. Yet, the independence of the association between the small dense LDL phenotype and CHD risk from other known risk factors remains speculative as this thesis has not been supported by most epidemiological studies. However, the fact that the LDL size phenotype has been characterized using a wide array of methods certainly represents a major limitation in our ability to reach definite conclusions on whether or not small dense LDL should be considered an independent risk factor. While most epidemiological studies have characterized LDL size by polyacrylamide gradient gel electrophoresis (PAGE) using a variable referred to as the LDL peak particle diameter, more recent studies have indicated that other characteristics of LDL, particularly the proportion and absolute levels of small LDL particles, are more strongly related to the risk of CHD than the LDL peak particle diameter [2]. It is suggested that several components of the LDL size phenotype should be measured concurrently in order to fully appreciate the impact of the small dense LDL phenotype on CHD risk. LDL particles have also been characterized using other methods such as Nuclear Magnetic Resonance (NMR) [3] and more recently by heparin-magnesium precipitation [4]. However, these methods show various degrees of concordance with measures derived from PAGE. Finally, although it has long been suggested that small dense LDL have a prolonged plasma residence time compared to larger LDL, thereby contributing to their increased atherogenicity, this hypothesis had never been formally tested *in vivo* in humans using tracer studies with stable isotopes. We have recently developed a new protocol to investigate the *in vivo* kinetics of LDL with various sizes, using a single intravenous bolus of [¹³C]-leucine. We show using this method that LDL in the smaller LDL density range (d 1.044-1.063 g/ml) are cleared at a much slower rate than LDL with a lower density (d 1.019-1.034 g/ml). These novel analyses will be discussed in detail.

Conclusions: While the inverse association between the small dense LDL and CHD risk is virtually indisputable, several issues remain to be further investigated. The most representative measure of the LDL size phenotype in terms of CHD risk has to be determined. The *in vivo* physiology of small dense LDL also needs to be better characterized, particularly in association with patho-physiological states such as obesity and the metabolic syndrome.

References

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Th-W54:2 WHY METUSELAH LIVED TO BE 969: LONGEVITY GENES AND A NOVEL LIPOPROTEIN CONNECTION

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Objective: The discovery that a single gene can confer longevity in lower species have led us to examine whether centenarians are over-represented with phenotype and genotype for exceptional longevity.

Methods: We recruited a genetically homogenous population of unrelated Ashkenazi Jews between the ages of 60 and 108 years (n=366). Individuals who lived independently at age ≥ 95 years were defined as centenarians, or having exceptional longevity (n=169). To validate the genetic and physiological findings we also recruited 222 offspring of subjects with exceptional longevity. We assessed their serum lipoproteins levels and lipoprotein particle size (by NMR), and determined the presence of the metabolic syndrome (by