n-3 POLYUNSATURATED FATTY ACIDS AND BONE DENSITY IN RENAL TRANSPLANT RECIPIENTS

Jørgensen Hanne Skou[1] hsjorgensen@clin.au.dk, Eide Ivar Anders[2], Hartmann Anders[2], Åsberg Anders[3], Christensen Jeppe Hagstrup[4], Schmidt Erik Berg[5], Godang Kristin[6], Bollerslev Jens[6], Svensson My[1]

[1]Dep. of Nephrology, Aarhus University Hospital, Aarhus, Denmark
[2]Dep. of Transplant Medicine, Section of Nephrology, Oslo University Hospital, Rikshospitalet, Oslo, Norway
[3]School of Pharmacy, University of Oslo, Oslo, Norway
[4]Dep. of Nephrology, Aalborg University Hospital, Aalborg, Denmark
[5]Dep. of Cardiology, Aalborg University Hospital, Aalborg, Denmark
[6]Dep. of Endocrinology, Oslo University Hospital, Rikshospitalet, Oslo, Norway
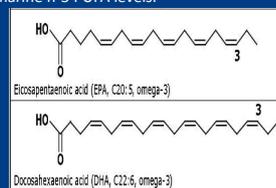
INTRODUCTION

Renal transplant recipients suffer high rates of bone loss and increased fracture-risk. Marine n-3 polyunsaturated fatty acids (n-3 PUFA) are essential fatty acids, found mainly in fish and seafood. n-3 PUFA may have beneficial effects on bone composition and are positively associated with bone mineral density (BMD) in healthy elderly. The aim of this study was to investigate if this association prevails in renal transplant recipients, despite the more complex causes of bone loss in these patients.
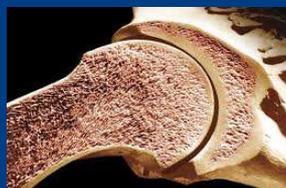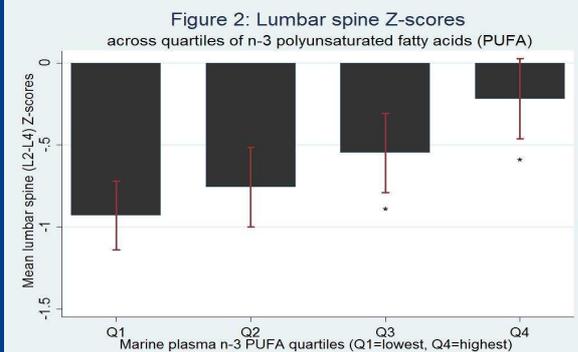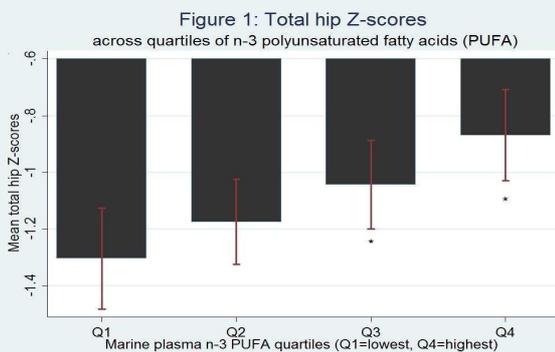
METHODS

A total of 701 renal transplant recipients were included in a cross-sectional analysis. BMD of lumbar spine, proximal femur and distal forearm were measured by dual energy x-ray absorptiometry (DEXA)-scan, and blood samples drawn in the fasting state for measurement of plasma fatty acid composition ten weeks post-transplant. Fatty acids were determined by gas chromatography, and expressed as weighted percent (wt%) of total plasma fatty acids. Multiple linear regression was used to assess the association between BMD and plasma marine n-3 PUFA levels.

RESULTS

Figure 1: Total hip Z-scores across quartiles of n-3 polyunsaturated fatty acids (PUFA)

Figure 2: Lumbar spine Z-scores across quartiles of n-3 polyunsaturated fatty acids (PUFA)

Median age was 53.9 [41.5, 64.0] years and two thirds (67.6%) were men. One third (28.1%) were transplanted pre-emptively, while the remaining had received renal replacement therapy for a median of 13.0 [7.8, 26.3] months. Mean eGFR (MDRD-equation) ten weeks post-transplant was 60.0 ml/min.

Median plasma marine n-3 PUFA was 7.6 [5.9, 9.8] wt%. Age (β = 0.009, $p < 0.001$) and plasma calcium (β = 0.206, $p = 0.02$) were positive, and active smoker (β = -0.123, $p < 0.001$), former smoker (β = -0.066, $p = 0.02$) and diabetic nephropathy (β = -0.107, $p = 0.001$) negative predictors of plasma n-3 PUFA levels.

Based on femoral neck T-scores, 26% of patients were osteoporotic and further 52% osteopenic. Z-scores increased significantly across quartiles of marine n-3 PUFA levels at all skeletal sites except the distal forearm (Figures 1 and 2).

Marine n-3 PUFA was a positive predictor of BMD at total hip and lumbar spine after multivariate adjustment (Table 1). No association was found between n-3 PUFA content and BMD of the distal forearm, nor between total n-6 PUFA and BMD at any site (data not shown).

Table 1: Multiple linear regression analyses with BMD (mg/cm²) as response and plasma marine n-3 PUFA (wt%) and potential confounders as explanantory variables

		β-coefficient	R²	p
Total hip	Age/gender adjusted	5.132	0.082	0.01
	Fully adjusted	**4.090**	**0.319**	**0.02**
Femoral neck	Age/gender adjusted	3.779	0.128	0.04
	Fully adjusted	2.721	0.313	0.09
Trochanter region	Age/gender adjusted	5.652	0.098	<0.01
	Fully adjusted	**4.474**	**0.315**	**<0.01**
Lumbar spine, L2-L4	Age/gender adjusted	4.374	0.034	0.12
	Fully adjusted	**5.825**	**0.187**	**0.02**
Fully adjusted model:	Age, gender, BMI, active smoker, diabetic nephropathy, dialysis vintage, se-iPTH, se-phosphate, prednisolon dose and first renal transplant			

MECHANISMS OF ACTION

Proposed mechanisms of n-3 PUFA on bone health include indirect effects through increased calcium-reabsorption in the intestine, as demonstrated by increased calcium transport across rat intestinal cells following treatment with marine n-3 PUFA. We found a positive correlation between plasma marine n-3 PUFA levels and p-calcium, which may support this hypothesis. Additionally, direct effects on bone turnover through effects on both bone formation and bone resorption have been reported. In an in vitro study of human mesenchymal stem cells, both EPA and DHA increased expression of osteoblast differentiation genes and of alkaline phosphatase. Several studies reported inhibition of osteoclast-function through the receptor activator of nuclear factor κβ ligand (RANKL)-RANK-osteoprotegerin (OPG) signaling pathway.
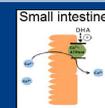
CONCLUSIONS

Plasma marine n-3 PUFA levels were positively associated with BMD at the hip and lumbar spine ten weeks post-transplant.
Marine n-3 PUFA supplementation may potentially improve bone density after renal transplantation.

CONFLICTS OF INTEREST

AARHUS UNIVERSITY