RETROSPECTIVE ANALYSIS OF BONE METABOLISM IN PATIENTS WAITING FOR SIMULTANEOUS PANCREAS KIDNEY TRANSPLANTATION

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INTRODUCTION:
Osteoporosis is a typical long-term complication after solid organ transplantation. Patients after **simultaneous pancreas kidney transplantation** (SPK) are at a very high risk due to preceding renal osteopathy and diabetic status and the risk of fracture is extraordinary elevated.

Pathogenesis:
The negative impact of **type 1 diabetes** (T1DM) is mediated through deficient insulin anabolic effect on osteoblasts, toxic impact of hyperglyceamia on osteoblasts, AGE´s cummulation in bone matrix, neuropathy, microangiopathy and calcium and magnesium loss due to polyuria. Moreover if diabetic nefropathy deteriorates into **chronic kidney disease** (CKD), bone impairment due to secondary hyperparathyreosis, hypocalcemia and vitamine D deficiency develops since CKD 2. Additional negative factors (malnutrition, immobilization, hypogonadism, medication…) may contribute to the bone loss.

OBJECTIVE:
To determine the best preventive strategy **we analysed the bone metabolism at the point of the pretransplant examination.**

DESIGN AND METHODS:
In years 2011-2014 the number of 112 patients with type 1 diabetes entered the waiting list for the SPK for the first time. We retrospectively analyzed **biochemical results** (Ca, P, iPTH, vitamin D 25-OH, 1,25-OH) and the **bone densitometry** (lumbal spine, proximal femur, distal radius T and Z score; Lunar Prodigy) from their pretransplant investigation (2010-2014). The densitometry was not available in 1 patient, the final analysis comprised 111 patients.

STATISTICAL ANALYSIS: Values are reported as means ± SD. The unpaired T test was used to compare the study subgroups. The Pearson correlation coefficient was performed to evaluate the associations between anthropometric and osteological parameters. P value ≤ 0,05 was considered statistically significant. GraphPad Prism 5 statistical sofrware was used for the data analysis.

RESULTS:

Characteristics of the study group

	Total (n = 111)	Men (n = 68)	Women (n = 43)	Significance
Age (years)	40,71 ± 10,44	42,93 ± 10,47	37,21 ± 9,49	P=0,004
DM duration (years)	24,69 ± 7,98	24,19 ± 7,73	25,49 ± 8,37	NS
BMI (kg/m2)	24,65 ± 3,48	25,22 ± 3,36	23,75 ± 3,51	P=0,03
HbA1c (mmol/mol)	73,07 ± 17,15	73,02 ± 14,82	73,05 ± 20,67	NS
GF (ml/s)	0,24 ± 0,12	0,26 ± 0,13	0,20 ± 0,1	P=0,014
CKD 4 (GF > 0,25ml/s)	44	33	11	
CKD 5 (GF < 0,25ml/s)	27	9	18	
CKD 5D (31 HD, 9 PD)	40	26	14	
Ca (mmol/l)	2,24 ± 0,27	2,28 ± 0,31	2,19 ± 0,17	NS (p=0,09)
P (mmol/l)	1,67 ± 0,36	1,62 ± 0,3	1,77 ± 0,43	P=0,03
iPTH (pmol/l)	19,05 ± 13,32	18,35 ± 12,86	20,2 ± 14,13	NS
25-OH vitamin D (ug/l) (n=84)	15,49 ± 7,67	15,59 ± 6,7	15,31 ± 9,3	NS
1,25-OH vitamin D (ug/l) (n=83)	19,3 ± 14,1	19,38 ± 13,42	19,12 ± 15,74	NS

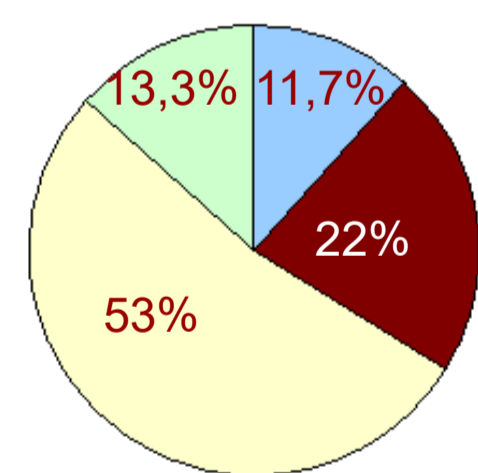24% of patients had **25-OH vitamin D deficiency** (<10ug/l), only 2% had normal level (>30ug/l).

Relationship between PTH and GF

Inadequately high levels

low levels

Bone mineral density

		Total (n=111)	Men (n=68)	Women (n=43)	Significance
LUMBAL SPINE	T	-0,94 ± 1,38	-1,19 ± 1,23	-0,54 ± 1,46	P = 0,015
	Z	-0,83 ± 1,42	-1,09 ± 1,29	-0,42 ± 1,54	P = 0,015
PROXIMAL FEMUR	T	-1,39 ± 1,12	-1,44 ± 1,00	-1,31 ± 1,27	NS
	Z	-1,16 ± 1,14	-1,19 ± 1,03	-1,10 ± 1,31	NS
DISTAL RADIUS (n=95)	T	-0,89 ± 1,01	-0,87 ± 1,06	-0,88 ± 0,98	NS
	Z	-0,80 ± 1,05	-0,82 ± 1,11	-0,78 ± 1,00	NS

Men have significantly lower BMD in lumbal spine than women.
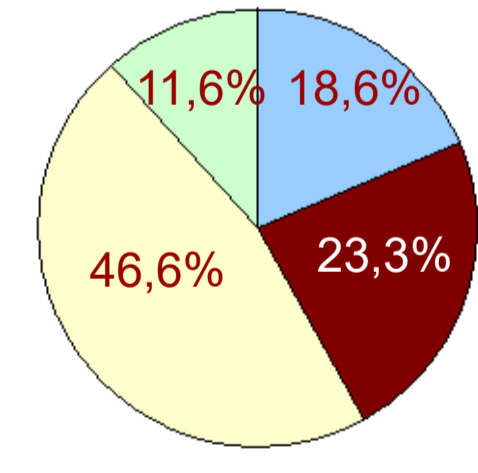T- and Z- score of the proximal femur is significantly lower than that of the lumbar spine or distal radius.
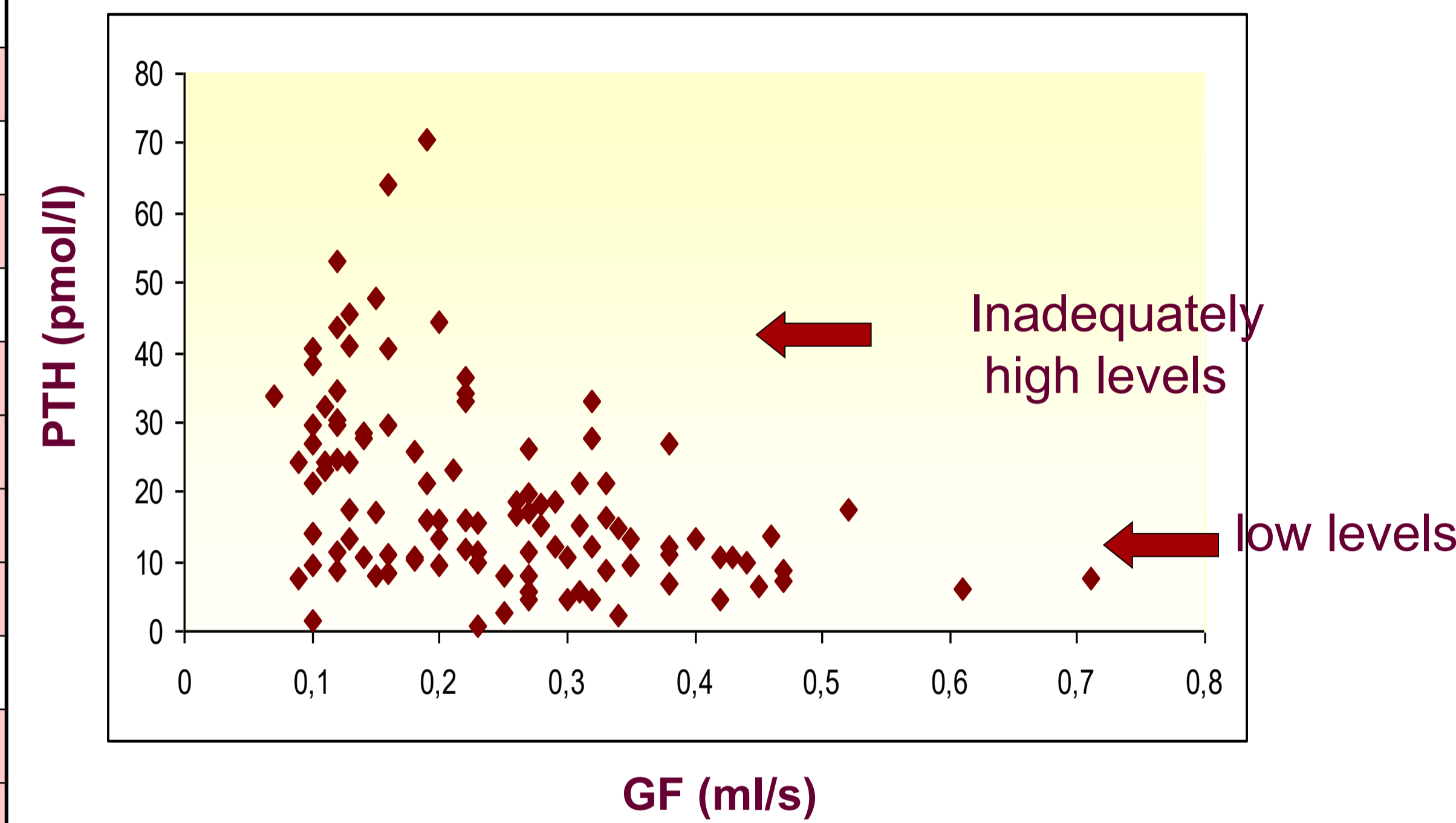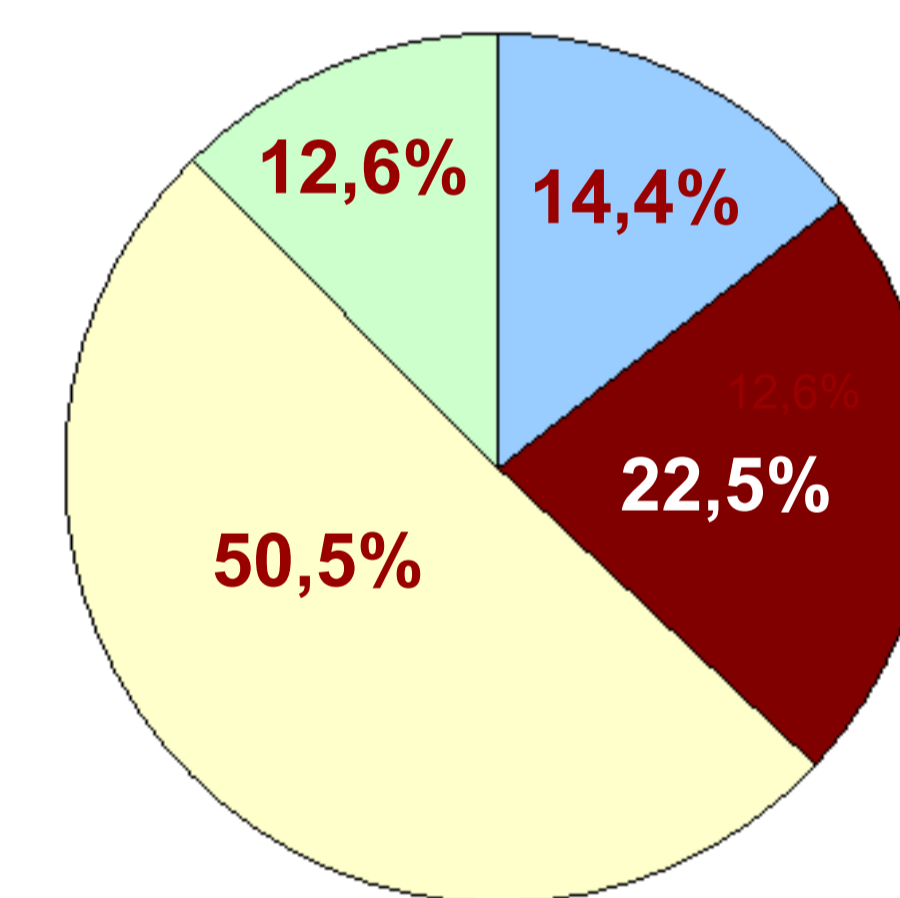
Bone mineral density (the whole group)

T skóre
< 2,5 OSTEOPOROSIS
< 1,0 OSTEOPENIA
< 0,5 LOW NORMAL BMD
≥ 0,5 NORMAL BMD

14,4% / 22,5% / 50,5% / 12,6%

High prevalence of osteoporosis and osteopenia in young patients.

Bone mineral density in subgroups

MEN (n=68) — 11,7% / 22% / 53% / 13,3%

WOMEN (n=43) — 18,6% / 23,3% / 46,6% / 11,6%

Similar prevalence of osteoporosis between men and women

CKD 5D (n=40) — 7,5% / 40% / 40% / 12,5%

CKD 4 (n=44) — 18,3% / 9% / 63,7% / 9%
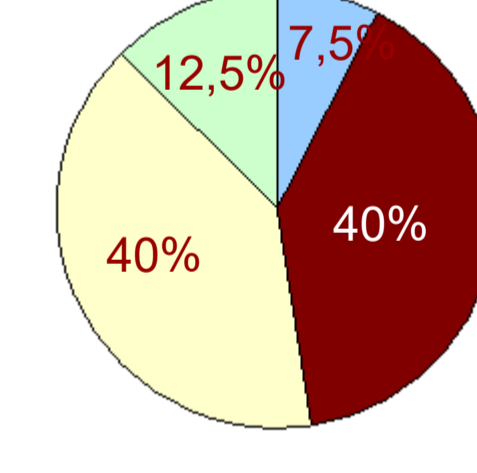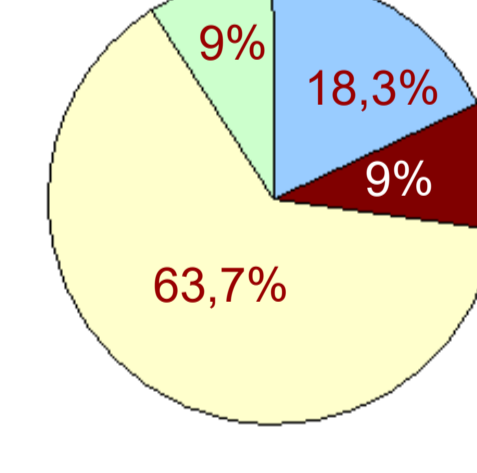
Substantially higher prevalence of osteoporosis among dialysed patients.

Correlations among BMD and anthropometric parameters

		BMI (kg/m2)	Age (years)	Duration of T1DM (years)	The age of T1DM diagnosis (years)
THE WHOLE STUDY GROUP (n=111)	LP (g/cm2)	r=0,31 (p<0,001)	r=0,22 (p=0,02)	r=0,18 (p=0,056)	r=0,08 (NS)
	PF (g/cm2)	r=0,46 (p<0,001)	r=0,24 (p=0,01)	r=0,1 (NS)	r=0,16 (NS)
MEN (n=68)	LP (g/cm2)	r=0,24 (p=0,054)	r=0,16 (NS)	r=0,16 (NS)	r=0,21 (NS)
	PF (g/cm2)	r=0,36 (p=0,002)	r=0,2 (NS)	r=0,2 (NS)	r=0,23 (p=0,058)
WOMEN (n=43)	LP (g/cm2)	r=0,48 (p<0,001)	r=0,43 (p=0,004)	r=0,46 (p=0,002)	r=-0,06 (NS)
	PF (g/cm2)	r=0,56 (p<0,001)	r=0,23 (NS)	r=0,32 (p=0,04)	r=-0,15 (NS)

Surprisingly positive correlation between BMD and age and BMD and the duration of diabetes.

BMD and the age of T1DM diagnosis

Z score

Lumbal spine — P = 0,07
Proximal femur — P = 0,03

Age under 15years (n=69)
later (n=42)

T1DM diagnosis in childhood and early adolescence negatively affects the peak bone mass with the impact for the rest of the life.

CONCLUSIONS: Patients with type 1 diabetes in CKD 3-5 suffer from serious bone mineral density impairment despite their young age. On contrast to population data the incidence of low bone density is the same among men and women. Proximal femur is the most affected area. Patients with type 1 diabetes since early childhood are at a very high risk of having low BMD.
Bone metabolism should be monitored since early stages of diabetic nephropathy and adequate preventive measures (sufficient vitamine D intake in the first place) should be introduced.