CKD BONE DISEASE

MP201 MANGANESUM PROMOTES OSTEOGENESIS OF MESENCHYMAL STEM CELLS VIA NOTCH SIGNALING

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Introduction and Aims: In clinical practice it has been reported that hypomagnesemia is associated to low mineral density. On the other hand in vitro studies have shown that magnesium (Mg) decreases calcification in vascular smooth muscle cells. But the effects of increasing Mg levels on bone homeostasis are poorly understood. Here we elucidate the effects of elevated Mg on the osteogenic differentiation of rat MSC and hence on bone metabolism.

Methods: MSC were differentiated to osteoblasts by incubation with dexamethasone, β-glycerol phosphate and ascorbic acid at different Mg concentrations. Mineralization capacity and osteoblastic markers were measured. Involvement of canonical Wnt and Notch signaling pathways in this process was analyzed by immunofluorescence. Inhibition of Mg channel TRPM7 by 2-aminoethoxydiphenyl borate (2-APB) was also studied.

Results: Elevated Mg increases matrix mineralization, alkaline phosphatase activity and FGF-23 production in rat MSC. Further, the expression of osteoblast master genes such as Runx2, Osterix and Osteocalcin was augmented (Table 1). No significant differences on nuclear translocation of β-catenin were observed. However, translocation of Notch1 intracellular domain (NICD) into the nuclei increased significantly in osteoblasts cultured with rising Mg concentrations. Further, Mg promoted proliferation induced by increasing CyclinD1 and PCNA levels. 2-APB administration decreased nuclear NICD, alkaline phosphatase activity, osteoblast master genes and proliferation marker expression.

Conclusions: Our data strongly suggest that Mg directly enhances osteogenesis in rat MSC.

Introduction and Aims: Severity of anemia was reported to be associated with 25-hydroxyvitamin D (25D) and 1,25-dihydroxyvitamin D (1,25D) levels in patients with CKD. However, it remains unclear which markers related to mineral bone disorders (MBD) predict the progression of anemia in this population.

Methods: In the OVIDS-CKD study, we prospectively followed temporal change of hemoglobin (hgb) levels. At baseline, we measured 6 MBD markers including intact FGF23, 1-84 parathyroid hormone (PTH), 25D, 1,25D, serum calcium, and phosphate. Out of 734 patients, we selected 571 patients not receiving erythropoietin stimulating agents (ESA) who had hgb ≥10 g/dL at baseline. We followed the patients until the start of ESA therapy, the day of transfusion, or the end of observation period, which comes first. First, we performed Cox proportional hazards model to examine which MBD markers predict the time to hgb <10 g/dL on the start of ESA therapy. Second, we employed a linear mixed effects model with hgb as a time-dependent outcome variable, adjusting for time-dependent eGFR, because renal function change partly determines the progression of anemia and is also predicted by MBD markers. The interaction term of time*each MBD marker was entered into the model to examine if these markers modify the relationship between time and hgb (hgb slope).

Results: Cox models revealed that out of 6 makers only 25D and FGF23 levels predicted the time to the outcome, in addition to prior CVD, proteinuria, baseline hgb, and eGFR. (adjusted HR per unit change of log FGF23 and 10 ng/mL of 25D 1.49 [1.13–1.97] and 0.53 [0.37–0.77], respectively). However, this finding is thing of course, given that FGF23 and 25 D predict renal outcome (Nakan C, CJASN2012), which determines the progression of anemia. Mixed effects model adjusting for time-dependent eGFR revealed that FGF23 and PTH levels were associated with faster decline of hgb (-0.06 [-0.10 to -0.02] g/dL/year and -0.05 [-0.09 to -0.01] g/dL/year per SD increase, respectively. Further adjustment by 1,25D extinguished the significance of FGF23, while it did not change the parameter estimate for PTH (-0.04 [-0.09 to -0.01] g/dL/year and -0.05 [-0.09 to -0.01] g/dL/year per SD increase, respectively).

Conclusions: Two phosphatonin predicts the progression of anemia in patients with CKD. FGF23 might predict the progression of anemia partly by suppressing the production of 1.25D.

Introduction and Aims: Two phosphatonin predict the progression of anemia in patients with CKD.

MP203 BONE MINERAL DENSITY BY CLINICAL CT IS ASSOCIATED WITH NON-VERTEBRAL FRACTURES IN RENAL TRANSPLANT CANDIDATES

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Introduction and Aims: Fracture-risk is increased 2-4 fold in chronic kidney disease (CKD). At present there is no consensus on how to identify patients at risk. Bone mineral density (BMD) by dual x-ray absorptiometry (DXA)-scan is not recommended, due to lack of a strong and consistent relationship with fractures in CKD, which may be due to the two-dimensional quality and low resolution. Computed tomography (CT) yields three-dimensional, high resolution images, and is widely used for diagnostic procedures. As spine and hips are often included in scans, a concomitant measurement of volumetric BMD (vBMD) is possible. We investigated the association between vBMD by clinical CT and fragility fractures in patients with CKD stage 5D.

Methods: We recruited adult renal transplant candidates from four centers in Denmark. As part of cardiac evaluation, patients underwent CT angiography. Scans were performed on a Siemens Somatom Definition Flash scanner, and included chest, abdomen and pelvis. A calibration phantom (InTable, Image Analysis) was included, and images were analyzed by dedicated software (QCT-Pro, Mindways Inc). Fracture status was determined by previous clinical fracture, classified as fragility fracture if resulting from a fall from standing height or less. All fractures were confirmed by chart review.

Results: A total of 113 patients had successful vBMD-analysis of both spine and hip. Eighty-two were men (72.6%) and 31 women (27.4%), with an average age of 54 years. Underlying diagnoses of kidney failure were: diabetes type 1 or 2 (43.3%), hypertension or glomerulosclerosis: 27 (23.9%), glomerulonephritis or vasculitis: 29 (25.7%), adult polycystic kidney disease: 14 (12.4%) and other: 11 (9.7%). Sixty-four patients (56.5%), were not yet on dialysis with an average eGFR of 12.8 ml/min. Thirteen (11.5%) received peritoneal dialysis, and 36 (31.9%) hemodialysis, for an average duration of 13 and 36 months respectively. Twenty patients (17.7%) had previously received a renal transplant. There were 41 fractures in 30 patients. Of those, 36

Table 1 - Levels of selected osteogenic markers

<table>
<thead>
<tr>
<th>Markers</th>
<th>UC</th>
<th>OB (0.5 mM Mg)</th>
<th>OB (1.2 mM Mg)</th>
<th>OB (1.8 mM Mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Runx2 (x-fold expression)</td>
<td>1.0 ± 0.23</td>
<td>5.2 ± 1.09a</td>
<td>41.1 ± 14.23a</td>
<td>219 ± 42.39a</td>
</tr>
<tr>
<td>Osteocalcin (x-fold expression)</td>
<td>1.4 ± 0.51</td>
<td>830 ± 123a</td>
<td>98649 ± 7048a</td>
<td>124847 ± 16875a</td>
</tr>
<tr>
<td>ALP activity (U/g protein)</td>
<td>1.0 ± 0.23</td>
<td>5.2 ± 1.09a</td>
<td>17.1 ± 2.10b</td>
<td>26.7 ± 1.80c</td>
</tr>
</tbody>
</table>

M202 TWO PHOSPHATINH HORMONES PREDICT THE PROGRESSION OF ANEMIA IN PATIENTS WITH CKD

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Introduction and Aims: Severity of anemia was reported to be associated with 25-hydroxyvitamin D (25D) and 1,25-dihydroxyvitamin D (1,25D) levels in patients with CKD.

Method: In the OVIDS-CKD study, we prospectively followed temporal change of hemoglobin (hgb) levels. At baseline, we measured 6 MBD markers including intact FGF23, 1-84 parathyroid hormone (PTH), 25D, 1,25D, serum calcium, and phosphate.

Results: Cox models revealed that out of 6 makers only 25D and FGF23 levels predicted the progression of anemia in patients with CKD. FGF23 might predict the progression of anemia partly by suppressing the production of 1,25D.

<table>
<thead>
<tr>
<th>Region</th>
<th>Fracture, mean (SD) mg/cc</th>
<th>No fracture, mean (SD) mg/cc</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar spine</td>
<td>115 (50.4)</td>
<td>128 (41.6)</td>
<td>0.30</td>
</tr>
<tr>
<td>Total hip</td>
<td>209 (31.3)</td>
<td>263 (48.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>201 (35.1)</td>
<td>261 (54.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Methods: We conducted clinical and biological studies including screening for mutations in the 13 exons of GNAS1 gene in 23 patients (mean age= 26.5±1.20; 17 male, 6 female) with SS. PTH, free T3, T4, TSH, calcitonin, ALP, CA, P, FSH, LH, total testosterone and vitamin D were evaluated. Evaluation for osteoporosis was made by total hip vBMD was 0.8416, and femoral neck vBMD 0.8226 (see figure). 

Conclusions: Hip vBMD, but not lumbar spine vBMD, by clinical CT angiography, was associated with previous non-vertebral fragility fracture in renal transplant candidates with CKD5-D5.

**Introduction and Aims:** Sakliker syndrome (SS) seems to be related to CKD, secondary hyperparathyroidism and uglifying human face appearances. The etiology of SS is not known, and is plausible to think that they are genetically predisposed. The genetics importance of GNAS1 gene mutations on outcome in patients with SS is unclear, and no search has addressed GNAS1 mutations. This is the first report on this topic. 

**Methods:** We sought to evaluate whether inflammation affects Sost levels in HD. To our knowledge this is the first report on this topic.

**Results:** 41 patients (59±16 y.o.) on HD since 5,9±4,8 y were sampled for Sost and parameters of inflammation (IL1, IL6, IL10, TNFα, OPG, RANKL,) and of mineral metabolism (Ca, P, PTH, Vit D). 30 healthy subjects (34±12 y.o.; eGFR 95±19 ml/min) served as control.

**Conclusions:** Our data confirm the increment of serum Sost in HD in a range similar to what has been already reported. Importantly the negative correlations with P and PTH are in agreement with a role of Sost on bone: the higher Sost, the lower bone turnover. The positive relationship between Sost and inflammatory cytokines points to a role of inflammation on bone, exerted through Sost. Conceivably inflammation, by increasing Sost, could negatively affect bone turnover, a modulatory effect already described in HD patients. Further, the positive correlation of Sost with age, OPG, RANKL, and the inflammatory cytokines suggest also a link with arteriosclerosis. In fact, Sost levels have been recently shown to correlate with vascular calcifications in HD patients.
HD In conclusion, the increase of Sost occurring in HD could be secondary, at least in part, to inflammation. Sost in this population can negatively affect bone turnover thus closing a circle linking inflammation and bone disease.

MP205 Mean values (±SD) of the evaluated parameters in the two populations are in the table

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HD (41)</th>
<th>Control (30)</th>
<th>p&lt;0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sost, nmol/l</td>
<td>59±16</td>
<td>28±10</td>
<td>0.001</td>
</tr>
<tr>
<td>OPG, ng/ml</td>
<td>5.3±3</td>
<td>1.0±0.2</td>
<td>0.001</td>
</tr>
<tr>
<td>RANKL, mcg/ml</td>
<td>4.7±4</td>
<td>3.0±0.5</td>
<td>0.001</td>
</tr>
<tr>
<td>IL-1, pg/ml</td>
<td>0.27±0.58</td>
<td>0.01±0.03</td>
<td>0.001</td>
</tr>
<tr>
<td>IL-6, pg/ml</td>
<td>12.1±9</td>
<td>3.0±0.3</td>
<td>0.001</td>
</tr>
<tr>
<td>IL-10, pg/ml</td>
<td>9.5±11.9</td>
<td>3.3±1.3</td>
<td>0.001</td>
</tr>
<tr>
<td>TNFα, pg/ml</td>
<td>13±11</td>
<td>3±2</td>
<td>0.001</td>
</tr>
<tr>
<td>PTH, pg/ml</td>
<td>34±363</td>
<td>3±4</td>
<td>0.001</td>
</tr>
<tr>
<td>Ca, mg/dl</td>
<td>8.9±0.9</td>
<td>9.6±0.4</td>
<td>0.001</td>
</tr>
<tr>
<td>P, mg/dl</td>
<td>4.7±1.5</td>
<td>3.8±0.6</td>
<td>0.001</td>
</tr>
<tr>
<td>25D, ng/ml</td>
<td>11.8±6.7</td>
<td>18±18</td>
<td>0.001</td>
</tr>
<tr>
<td>L25D, pg/ml</td>
<td>11.1±15.4</td>
<td>56±12</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Introduction and Aims: An altered bone remodeling is observed in subjects with progressive loss in renal function, particularly in patients with CKD requiring dialysis (stage 5D), and in the majority of patients with CKD stages 3-5. Cytokines can act as autocrine factors regulating osteoblast/osteoclast (OCs) cells functions. In pathological conditions, immune cells and inflammatory cytokines belonging to tumor necrosis factor superfamily, such as LIGHT and RANKL, play a key role in osteoclastogenesis. The aim of our study was to evaluate the osteoclastogenic potential of unfractionated and T cell-depleted PBMCs from CKD and hemodialysis (HD) patients.

Methods: OCs obtained from freshly unfractionated and T cell-depleted PBMCs of CKD patients, were cultured for 21-25 days with and without exogenous cytokines (rh-MCSF and RANKL). Mature OCs were identified as tartrate resistant acid phosphatase (TRAP)+ multinucleated cells containing 3 or more nuclei. The presence of circulating osteoclast precursors (CD14++CD16+) and the LIGHT and RANKL expression in the immune cell subset were evaluated through the flow cytometry. Serum levels of CTX (carboxy-terminal collagen type I), a new marker of osteoclastogenesis, were measured.

Results: PBMCs from HD and CKD patients showed a spontaneous osteoclastogenesis in vitro (80±5%/well). Conversely, exogenous cytokines were essential to trigger and sustain osteoclastogenesis in CKD patients (stage I-II) and controls (10±4%/well). This process was correlated with a significant increase of both LIGHT and RANKL expression on CD4+ T cells as well as CD14+CD16+ monocytes, particularly in HD and CKD patients (stage III-V) compared to controls (p<0.005). The increase of these inflammatory cytokines and CD14+CD16+ monocytes was associated with an increase in serum levels of CTX both in HD and CKD pts (stage IV-V) compared to controls (p<0.005).

Conclusions: In conclusion, under inflammation conditions, uremic PBMC show an increased osteoclastogenic potential that may play a role in the mineral bone disorder observed in CKD patients. Modulation of LIGHT and RANKL expression may represent a new potential therapeutic target in the setting of these patients.

MP207 SCLEROSTIN SERUM LEVELS AND VASCULAR CALCIFICATION IN PREVALENT RENAL TRANSPLANT RECIPIENTS: A LONGITUDINAL COHORT STUDY

Peter Evenepoel1, Eric Goffin2, Björn Meijers1, Nada Kanaan2, Bert Bammens1, Emmanuel Coche2, Kathleen Claes1 and Michel Jadoul2

Introduction and Aims: Vascular calcification (VC) is prevalent and progressive in renal transplant recipients. The present study aimed to test the hypothesis that sclerostin, a Wnt antagonist produced by osteocytes, might protect against progression of vascular calcification (VC).

Methods: This is an extension of the previously reported longitudinal observational Brussels Renal Transplant Cohort study. Coronary artery (CAC) and aortic calcification (AoC) was measured by multislice spiral CT in 208 prevalent renal transplant recipients. A repeat scan was available in 189 patients after a median follow-up of 4.4 years. In addition to traditional and non-traditional risk factors, baseline serum sclerostin levels (Telemedical) were assessed on stored blood samples. Regression analysis was performed to identify determinants of baseline VC and progression.

Results: VC was present in up to 84% of patients at baseline. Almost half of the patients showed progression of VC, according to Hokanson criteria. The cross-sectional analysis demonstrated a direct association at baseline between sclerostin and VC score in univariate analysis, which became inverse after adjustment for age, gender and PTH level. Remarkably, a lower sclerostin level was identified as an independent determinant of a higher baseline AoC score in the final regression model. The longitudinal cohort study showed an inverse association between baseline sclerostin levels and VC progression, but significance was lost in most final models. Baseline VC is the most important risk factor for future progression.

Conclusions: Sclerostin levels inversely associated with vascular calcification burden and progression in prevalent renal transplant recipients after adjustment for traditional risk factors. These data refer the previous findings in non-transplanted CKD patients and support the thesis that sclerostin is up-regulated in the vascular wall during the vascular calcification process as part of a local counter regulatory mechanism directed to suppress vascular calcification.
the Modification of Diet in Renal Disease formula, renal diagnosis, bone density measurements including T-scores and Z-scores for the lumbar spine, both hips, and the one-third distal radius, as well as the number of fractures. We compared these measures across patients in CKD Stages 2 through 5 for total hip and femoral neck bone density (T<.001). Increasing serum phosphorus was significantly associated with reduced bone mineral density as CKD progresses.

Results: We found a significant decline in mean bone density across Stages 2 through 5 for total hip (X2 (3) = 16.73, p<.001) and femoral neck (X2 (3) = 12.76, p=.005) sites, but not lumbar spine or one-third distal radius. The most prominent differences were between Stages 2 and 3 and Stage 5. This decline was similar across CKD stages for both males and females but females generally had lower bone density overall. Similar results were found using bone mineral density T-Scores and Z-Scores. We also found associations between CKD stage progression from 2 to 5 and reductions in serum calcium (X2 (3) = 38.96, p<.001) and increases in serum phosphorus (X2 (3) = 81.93, p<.001). Increasing serum phosphorus was significantly associated with reduced bone mineral density in the total hip (r=-.15, p<.05, Spearman’s rho) and tended towards significance for femoral neck (r=-.10, p=.056, Spearman’s rho). The percentage of patients suffering from a fracture, however, did not significantly change with CKD stage using a between-groups analysis (X2 (3) = 6.42, p=.09, Cramer’s V = .3, p=.09).

Conclusions: There is a demonstrable decline in total hip and femoral neck bone density with progression of CKD staging. In contrast, lumbar spine and distal radius bone mineral density were not affected by CKD stage. Although DXA scan data can provide information on BMD, they do not comment on trabecular and cortical microarchitecture and the resolution is too low to distinguish between cortical and trabecular bone. Future research will determine whether decreased bone density as determined by DXA scan is associated with increased fracture risk over time in the same patients. We will also examine the effect of treatment with bisphosphonates on BMD as CKD progresses.

Introduction and Aims: In recent years, medical therapies (vitamin D analog or calcimimetics) have led to a decline in surgical parathyroidectomy (PTx) among hemodialysis patients. However, this procedure is not uncommon in some DOPPS countries, ranging from 2.0 (Japan) to 14.3 (Canada) PTx per 1000 patient years. Therefore, this study aimed to determine factors that influence surgical parathyroidectomy for more than 5 years.

Methods: 558 patients, from 1996-2011, in N America, Europe, Australia, New Zealand, and Japan were included. These patients underwent PTx during the study period and had a history of prior PTx. Serum calcium and phosphorus were collected monthly; PTH and medication prescriptions were collected every 4 months. Serum concentrations of PH, calcium, and phosphorus were examined over the 3 months prior to and 12 months after PTx.

Results: Median PH levels dropped dramatically from 1100 pg/ml in the month before to 70 pg/ml 3 months after PTx, and remained low in the year after surgery (median: 579 pg/ml). 45% of patients had PH levels < 60 pg/ml in the months after surgery (figure). The percentage of patients with PH levels 50-300 pg/ml was 31% to 37% in the year after surgery, while the percentage of patients with PH levels < 30 ng/ml 300-600 pg/ml was 6% to 10%. Serum calcium levels dropped after PTx, with 36% of patients having < 8 mg/dl at month 3, and 19% < 8 mg/dl at month 12 (figure). Results were consistent and similar when using albumin-corrected calcium. One year after surgery, 82% of patients were receiving a calcium supplement or calcium-based phosphate binder vs. 58% of patients 3 months prior to surgery. Vitamin D (oral and IV) use 3 months prior to surgery was 66% and remained relatively stable in the year after surgery (60 to 73%). Cinacalcet use decreased from 23% before surgery to < 10% in the year after surgery. Mean per cent changes of PH levels decreased 2.0 mg/dl in the month prior to surgery to 4.1 mg/dl in the month after surgery, and ranged from 3.5 to 5.7 mg/dl in months 4 to 12 after surgery.

Conclusions: PTX resulted in striking reduction of PTH, with most postoperative concentrations below current clinical guidelines. Additionally, very low calcium levels persisted for 12 months following PTX in a notable proportion of patients and required medical management. The possibility of severe and persistent post-operative hypocalcemia should be taken into account when considering surgical versus medical treatment options for hyperparathyroidism.

SEVERE HYPOCALCEMIA PERSISTS IN THE YEAR AFTER PARATHYROIDECTOMY: RESULTS FROM THE DIALYSIS OUTCOMES AND PRACTICE PATTERN STUDY

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Introduction and Aims: Hyperparathyroidism is one of serious complications for continuous hemodialysis patients. However, procedure is not uncommon in some DOPPS countries, ranging from 2.0 (Japan) to 14.3 (Canada) PTx per 1000 patient years. Therefore, this study aimed to determine factors that influence surgical parathyroidectomy for more than 5 years.

Methods: 558 patients, from 1996-2011, in N America, Europe, Australia, New Zealand, and Japan were included. These patients underwent PTx during the study period and had a history of prior PTx. Serum calcium and phosphorus were collected monthly; PTH and medication prescriptions were collected every 4 months. Serum concentrations of PH, calcium, and phosphorus were examined over the 3 months prior to and 12 months after PTx.

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Conclusions: PTX resulted in striking reduction of PTH, with most postoperative concentrations below current clinical guidelines. Additionally, very low calcium levels persisted for 12 months following PTX in a notable proportion of patients and required medical management. The possibility of severe and persistent post-operative hypocalcemia should be taken into account when considering surgical versus medical treatment options for hyperparathyroidism.
and in 17.6% patients supernumerary gland (more than 5 glands) were removed at initial operation. 5. Total glandular weight and weight of the largest gland has gradually decreased in all Era. After PTx serum CaP and PTH levels were overall stable in all Era.7, 10.6% patients required removal of autograft for recurrent HPT and in 3.6% patients resection of missed gland for persistent HPT was performed. 8. Only three patients died during one month after PTx and complications, ie husky voice were negligible. 9, 10 years and 20 years patient's survivals after PTx were 83.1% and 61.9%.

Conclusions: PTx for HD patients with advanced SHPT was safe and effective treatment and should be selected before irreversible events are progressive.

**MP215**

**SCLEROSTIN A POTENTIAL MARKER OF RECOVERY FROM SECONDARY HYPERPARATHYROIDISM AFTER KIDNEY TRANSPLANTATION**

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1Medical University of prof. dr. J. H. Krzysztof Kowalski; 2Regional Hospital, Poznań, Poland

**Introduction and Aims:** Sclerostin is a 22 kDa glycoprotein secreted almost exclusively by osteocytes that inhibits Wnt/β-catenin signaling pathway, thereby decreasing bone formation and osteoblastogenesis. Osteoblast-stimulating actions of PTH are mediated by suppression of sclerostin. Sclerostin is much less accumulated in end-stage kidney disease as FGF-23 and its secretion and action are not directly related to phosphate metabolism. Therefore sclerostin may better reflect bone metabolism and recovery from secondary hyperparathyroidism (SHPT). The aim of the study was to analyze the effects of the changes of serum PTH and osteocyte products - sclerostin and FGF-23 on osteoblast function as determined by serum bone alkaline phosphatase (BAP) for 9 months after successful kidney transplantation (KTx).

**Methods:** Thirty five patients immediately after KTx from a deceased donor were included into 9-month observational study (17M, 18F, age 49±11 years, BMI 25±4, time on dialysis 27±13 months). Blood for measurement of serum creatinine, Ca, P, 25OHD vitamin D, PTH, FGF-23, sclerostin and BAP was taken immediately before KTx and 1 and 2 weeks, and 1,2,3,4,5,6 and 9 months thereafter.

**Results:** The results are shown in the table. At time of KTx serum FGF-23 correlated only with serum phosphate (r=0.62, p=0.01) and serum PTH with BAP (r=-0.48, p=0.04) but not with serum sclerostin. At the end of observation period neither serum sclerostin nor FGF-23 correlated with other parameters of mineral and bone metabolism.

**Conclusions:** Both sclerostin and FGF-23 have limited utility as markers of the resolution of SHPT and bone metabolism after KTx.

**MP214**

**EFFECTS OF PREOPERATIVE CINACALCET HYDROCHLORIDE (CH) TREATMENT ON OPERATIVE COURSE OF PARATHYROIDECTOMY (PTX) AND PATHOLOGICAL CHANGES OF RESECTED PARATHYROID GLANDS (PTGS)**

Ako Kakehashi1, Hiroaki Ogata1, Masahiro Yamamoto1, Hitotoshro1,1, Eriko Kirugasa1 and Yoshiyuki Kadoyama1

1Showa University Northern Yokohama Hospital, Yokohama, Japan

**Introduction and Aims:** Secondary hyperparathyroidism (SHPT) is associated with higher cardiovascular risk and mortality in dialysis population. CH, which has been clinically available in Japan since 2008, could reduce PTH levels effectively even in patients with severe SHPT refractory to CH.

**Objectives:** We retrospectively analyzed a total of 193 PTx for SHPT in long-term hemodialysis patients from April 2002 to December 2012 in Showa University Northern Yokohama Hospital.

**Methods:** We retrospectively analyzed a total of 193 patients with SHPT. SHPT was performed in patients with severe SHPT refractory to CH. Patients were exposed to 3 to 15 g/day CH for up to one year. Adverse Events (TEAE), 93.9% pts treated with calcium binders and 90.5% treated with phosphate binder, 49 pts calcium based phosphate binder alone and 169 sevelamer (SEV). Over 60% pts in every group were <65 yrs old, 106 pts (over 5%) were 75 yrs old or above. We show a combined safety analysis profile of CH in 12 phase II and clinical trials. All patients randomised presented with Chronic Kidney Disease Stage 5D with hyperphosphatemia. 163 pts received calcitriol alone, 47 pts calcitriol plus calcium phosphate binder, 49 pts calcium based phosphate binder alone and 169 sevelamer (SEV). Over 60% pts in every group were <65 yrs old, 106 pts (over 5%) were 75 yrs old or above.

**Results:** Overall 75% pts treated with CH reported one or more Treatment Emergent Adverse Events (TEAE), 93.9% pts treated with calcium binders and 90.5% treated with phosphate binders.

**Conclusions:** Most frequent TEAEs for both CH and SEV pts were GI disorders - nausea, vomiting, diarrhea, dyspepsia, constipation and abdominal pain. Incidence was 53.8% in SEV pts and 45.1% CH pts. For CH, in terms of severity, 26% were mild, 36.9% were moderate and 12.2% severe, as opposed to 32.0%, 42.6% and 16.0% for SEV. In terms of incidence, 26% were mild, 36.9% were moderate and 12.2% severe, as opposed to 32.0%, 42.6% and 16.0% for SEV. In terms of severity, 26% were mild, 36.9% were moderate and 12.2% severe, as opposed to 32.0%, 42.6% and 16.0% for SEV. In terms of severity, 26% were mild, 36.9% were moderate and 12.2% severe, as opposed to 32.0%, 42.6% and 16.0% for SEV.

**Conclusions:** The safety profile of CH is as expected for a nonabsorbed bile acid sequestant that has been shown to be an effective phosphate binder with additional potential benefits in hyperlipidemic, hypertensive and hyperglycemic patients. We show a combined safety analysis profile of CH in 12 phase II and III clinical trials. We report on the prospectively collected data from 12 phase II and III clinical trials. All patients randomised presented with Chronic Kidney Disease Stage 5D with hyperphosphatemia. 163 pts received calcitriol alone, 47 pts calcitriol plus calcium phosphate binder, 49 pts calcium based phosphate binder alone and 169 sevelamer (SEV). Only 12.2% severe, as opposed to 32.0%, 42.6% and 16.0% for SEV.

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attribute to impaired GH signaling pathway in liver and skeletal muscle leading to reduced insulin-like growth factor I (IGF-I). We have previously shown that linear growth impairment in CKD can also be explained by impaired long bone epiphyseal growth plate (rGH) GH receptor signaling. We have also recently shown that endurance exercise improves IGF architecture and IGF-1 content in a rat model CKD. Recombinant human growth hormone (rGH) treatment has been used to improve height in children with CKD, but GH effects on bone organization are poorly understood. In the present study we aimed to check the effects of GH treatment combined with treadmill exercise on the epiphyseal growth plate. 

Methods: 20 days old male SPD rats underwent a 2-stage 5/6 nephrectomy (CKD group) while control group was sham operated (C). The CKD group was further divided to 3 groups:1. (CKD) - receiving daily saline.2. (CKDgh) - receiving daily rGH (5mg/kg SC).3. (CKDgh + run) - receiving rGH plus 30 minutes of treadmill exercise at 17 m/min at 15° elevation.

Results: Animals were sacrificed 14 days after the induction of CKD. Tibia and femur were isolated for morphological analysis, real time PCR analysis of different bone markers (proliferative chondrocytes: Sox9, Collagen type II, Aggrecan; hypertrophic chondrocytes: Runx2, Collagen type X; fully differentiated hypertrophic chondrocytes: RANKL, MMP3, osteoblasts: Runx2, MMP13; Osteocalcin: RANKL).

Results: Body length, tail length and tibia length gain were all significantly reduced in CKD rats compared to C. GH treatment alone or combined with exercise did not improve these parameters. All CKD groups ate less food than C, but treatment with GH or exercise did not change food consumption compared to CKD. Growth plate IGF-I mRNA levels decreased in CKD while treatment with GH showed increased IGF-I mRNA levels in CKDgh and CKDgh + run compared to the same extent. SOX9, Aggrecan, Collagen type II and type X mRNA were all significantly increased in all CKD groups compared to C, but were even more significantly increased in CKDgh + run compared to the other CKD groups. Interestingly, Runx2 and MMP13 mRNA decreased in CKD and CKDgh while there was significant increase in CKDgh + run compared to C. Furthermore, RANKL mRNA decreased in CKD, rGH corrected this decrease to the levels of C and in CKDgh + run there was significant increase compared to C.

Conclusions: Longitudinal growth was not increased following rGH treatment alone or combined with exercise in this model of CKD related growth retardation, mainly due to the short term of the experiment. However, the obtained GH-exercise intervention showed potential beneficial effects on markers of differentiation towards more mature hypertrophic chondrocytes, which are responsible for normal growth through enchondral ossification.

MP217 OSTEONECTIN (SPARC) EXPRESSION IN VASCULAR CALCIFICATION: IN VITRO AND EX VIVO STUDIES

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Introduction and Aims: Osteonectin, also termed SPARC, is a major non collagenous protein of bone matrix and is associated generally with remodeling of tissues, mineralization, angiogenesis, and pathological responses to injury. Since there are controversial results regarding its role during the process of vascular calcification, we investigated osteonectin expression in our in vitro calcification model of rat vascular smooth muscle cells (VSMCs) challenged with high-phosphate (5 mM Pi).

Methods: Through immunohistochemical studies, we detected a peak of osteonectin expression at day 7 in cell treated with high-phosphate (high-Pi).

Results: According to the expression of osteonectin, the time course of calcium deposition, analyzed by von Kossa staining, resulted more apparent at day 7. On the contrary, the expression of the mitotic marker Ki-67 had a peak at day 4 showing a correlation of osteonectin only with calcium deposition and not with cell proliferation. Furthermore, ascorbic acid, a factor that potentiates high-Pi induced vascular calcification in our model, increased osteonectin expression, supporting a pro-calcifying role for its protein. Next we decided to study osteonectin expression ex-vivo in embryos, adult not calcified, and calcific vessels. Immunohistochemistry studies demonstrated a spread and strong reactivity in VSMCs of a 20 weeks fetus, confirming its potential role in regulation of mitosis and in cell differentiation. In not calcified arteries and in sclerotic aorta osteonectin expression was significantly reduced up to disappear in calcific plaques, where VSMCs were totally replaced. On the contrary, osteonectin was still present in VSMCs in close anatomic proximity to fatty streak lesions or overt calcification, where it could have a regulatory role in the calcification process.

Conclusions: Our in vitro and ex vivo data show osteonectin expression during the calcification process and suggest its potential role as pro-calcifying factor.

MP218 EFFECTS OF PYROPHOSPHATE DELIVERY IN A PERITONEAL DIALYSIS SOLUTION ON BONE TISSUE OF APOLIPROTEIN-E KNOCKOUT MICE WITH CHRONIC KIDNEY DISEASE

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Introduction and Aims: Vascular calcification (VC) is a risk factor for cardiovascular mortality in the setting of chronic kidney disease (CKD). Pyrophosphate (Pi), an endogenous molecule that inhibits hydroxyapatite crystal formation, has been shown to prevent the development of VC in animal models of CKD. However, the possibility of harmful effects of exogenous administration of Pi on bone requires further investigation. To this end, we examined by histomorphometry the bone of CKD mice after intraperitoneal Pi administration.

Methods: After CKD creation or sham surgery, 10-week-old female apolipoprotein-E knockout (apoE/-) mice were randomized to one non-CKD group or 4 CKD groups (n = 10-35/group) treated with placebo or three distinct doses of Pi and fed with standard diet. Eight weeks later, the animals were killed. Serum and femurs were sampled. Femurs were processed for bone histomorphometry.

Results: Placebo-treated CKD mice had significantly higher values of osteoid volume, osteoid surface and bone formation rate than sham- placebo mice with normal renal function. Slightly higher osteoid values were observed in CKD mice in response to very low Pi dose (OV/BV, O.Th and O.bl/S/B) and, for one parameter measured, to high Pi dose (O.Th), compared to placebo-treated CKD mice. Treatment with Pi did not modify any other structural parameters. Mineralization rates, other parameters of bone formation and resorption were not significantly different among the treated animal groups or control group.

Conclusions: In conclusion, Pi does not appear to be deleterious to bone tissue in apoE/- mice with CKD, although a possible stimulatory Pi effect on osteoid formation may be worth further investigation.
Introduction and Aims: Post TX HPSH can be considered to result, at least partly, from decreased expression of CaSR and VdD receptors on parathyroid cells. Receptor activators like CM or PC could increase expression of both and in this way improve clinical control. CM is used in HPSH with partial efficacy and some warnings (hypercalcemia, interference with immunosuppressive drugs, relapse after discontinuation). PC is less frequently employed but should theoretically suppress PTH without further increasing serum Ca and Pi. We hypothesized that, after normalization of serum Ca with the use of CM in TX suffering HPSH, PC could maintain PTH suppression without relapse of hypercalcemia if CaSR had been sufficiently increased.

Methods: Our prospective, randomized study enrolled pts with HPSH to receive CM for 1 month, titrating the dose for normocalcemia. Only responders were then randomized to continue on CM or to shift to PC for 3 months. Drug doses were aimed at normal serum Ca. Eight cases per group were calculated to be necessary for statistic purposes.

Results: Of 19 enrolled, 16 pts (54±7 y.o.; eGFR 58±20 ml/min, TX since 7±5 yrs) completed the study. Biochemical assays of serum Cr, Ca, Pi, PTH, BALP, 1,25D, FGF23 and Urine Ca/Cr were scheduled basally, after 1 month CM (All patients, mean administered dose 35±12 mg/day) and then after 3 further months of CM (Group A; 8 pts; mean dose 41±15 mg/day) or PC (Group B; 8 pts; mean dose 0.8±0.3 μg/day). One month of CM reduced serum Ca, PTH and FGF23 and increased Pi (table). After 3 months there was no further biochemical change in Group A, and an increment of serum Ca (back to basal, pre-treatment, values) and persistence of reduced PTH in Group B.

Conclusions: Thus, we can confirm the lowering effect of CaM on Ca and PTH in HPSH and report that FGF23 can decrease contemporarily to serum Pi increments in TX pts. PC similarly suppresses PTH but does not maintain reduced serum Ca, suggesting that the effect of CaM to occur CaSR stimulation were more relevant than increments of its expression. Our study underlines the role receptors and suggests that contemporary administration of CaM and PC could be advantageous to control HPSH in TX.

IMPAIRED ENDOTHELIAL FUNCTION AND MYOCARDIAL PERFUSION IN EXPERIMENTAL CHRONIC KIDNEY DISEASE

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Introduction and Aims: Cardiovascular causes account for approximately 50% of mortality in patients with chronic kidney disease (CKD). Among others, FGF23, a phosphate-lowering protein and elevated in CKD, and klotho, a cofactor for the FGF23 receptor and decreased in CKD are proposed determinants of cardiovascular risk in CKD. We hypothesise that renal failure results in impaired cardiovascular function and myocardial perfusion.

Methods: Eight-week-old male C57Bl/6 mice underwent partial nephrectomy (5/6Nx) to induce CKD, or sham-surgery. After 6 weeks, mice were placed into individual metabolic cages for 24 hours. Myocardial perfusion was assessed in vivo by myocardial contrast echocardiography (MCE) and ex vivo microvascular reactivity by pressure myography.

Results: 5/6Nx mice showed elevated levels of plasma urea (2.5-fold, p<0.001) and creatinine (2.3-fold, p<0.001) compared to baseline, and increased water intake (1.9-fold, p<0.001) and urine production (4.2-fold, p<0.001) compared to sham mice, all indicating renal failure. Plasma FGF23 significantly increased after Nx surgery (14-fold, p<0.01) and renal klotho mRNA expression was downregulated (P<0.05). As indication for a cardiac axis, 5/6Nx mice increased their heart weight/body weight ratio (p<0.01). In addition, 5/6Nx mice showed reduced myocardial blood volume during acetylcholine infusion (-18%, p<0.01), reduced microvascular filling velocity during sodium nitroprusside (SNP) infusion (-39%, p=0.06) and reduced myocardial perfusion during SNP infusion (p<0.05, -51%). Finally, 5/6Nx blunted ex vivo vasodilator responses to acetylcholine (<p<0.05), whereas responses to SNP or endothelin were normal.

Conclusions: This 5/6 Nx mouse-model shows distinct features of renal failure, among which increased plasma urea and creatinine levels. Perfusion defects are observed after kidney disease induction, as showed by a diminished myocardial perfusion in vivo, and a reduced ex vivo endothelial function. This is accompanied by highly increased plasma FGF23 levels and decreased renal klotho expression in these mice. All together, these results show the existence of a strong cardiorenal axis.
and death in a large cohort of prevalent patients on hemodialysis from south east Romania, a typical Balkan region.

Methods: This is an observational prospective study which included a total of 570 patients on maintenance hemodialysis. We included all patients with measured 25(OH)D, the baseline of our study. The patients were followed for a period of 14 months (between 01.09.2010 - 31.12.2011). Study patients were classified into three groups by baseline 25(OH)D levels: 1) sufficient 25(OH)D - i.e.<30 mg/ml, 2) insufficient 25(OH)D - i.e. between 10 mg/ml and 29 mg/ml and 3) deficient 25(OH)D - i.e.<10 mg/ml. Differences in survival at the end of the follow-up period were assessed with Log-rank test and Kaplan-Meier curves. We also performed a multivariate analysis of all-cause mortality using Cox proportional hazard models after adjusting for demographic data (age, gender), comorbid conditions and diagnosis and vitamin status.

Results: During the follow up period of 14 months, 68 patients (11.9%) died, the Kaplan-Meier analysis showing significant differences in all-cause mortality for CKD patients in the different 25(OH)D groups (p=0.002). Unadjusted Cox regression analysis also showed significant differences in survival. Compared to the >30 mg/ml group (HR) for death in the group with vitamin D levels <10 mg/ml was 2.572 (CI 95%: 1.37-4.94, p = 0.005). The multivariate Cox regression model showed no significant differences in survival according to vitamin D levels. HR for death in the ><10 mg/ml group was 1.823 (CI 95%: 0.928-3.579, p = 0.081) and in the 10-30 mg/ml group was 0.944 (CI 0.495-1.801, p = 0.861).

Conclusions: In our dialysis population with a high comorbidity burden, low 25(OH)D concentration was not associated with mortality in the adjusted Cox model, suggesting that vitamin D deficiency could represent only a non-specific marker for a poor health status, with less impact on mortality.

MP222 HELIO THERAPY IS EFFECTIVE FOR VITAMIN D IN ESKD PATIENTS
Rolfdieter Krause1,2, Heinrich Kaase3, Rainer Stange1, Werner Hopfenmüller1, Tai Otsuka1,2, Heinrich Kaase3, Rainer Stange1, Werner Hopfenmüller1, Taisover one year. The patients with age of older than 20 who firstly visited or were referred levels at the initial visit to nephrology centers with progression of renal dysfunction.

Results: After 6 months there was a significant increase and normalization of all vitamin D concentration. (dose-response-curve) were calculated. - Additionally in 6 patients skin biopsies were performed to determine vitamin D levels at the initial visit. The skin biopsies show the typical activation by uremic skin.

Introduction and Aims: The aim of this study was to investigate the circulating vitamin D metabolites after serial suberythemal irradiation with a sun-simulating UV spectrum and the vitamin D 25-dihydroxyvitamin D3, 1,25-dihydroxyvitamin D3 and 24,25-dihydroxyvitamin D3, which are the major vitamin D metabolites in the human body. All vitamin D metabolites increase into the normal ranges. Uremic skin is able to express VDR, 25- and 1-alpha-hydroxylase. - Therefore, serial heliotherapy is as effective as oral and/or intravenous application of vitamin D in patients with CKD.

Methods: We retrospectively analyzed data of CKD patients who have checked 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D simultaneously from March 2009 to March 2013. We enrolled patients aged between 20 and 80 years and excluded CKD patients with stage 1, 2.

Results: The percentage of patients with 25-hydroxyvitamin D levels < 20 ng/ml was 73% and the percentage of patients with 1,25-dihydroxyvitamin D levels < 25 pg/ml was 15.9%. Patients taking omega-3 fatty acids were 32 cases (CKD stage 3 : 81.3%). There was no significant difference of age (59.8 ± 12.7 vs. 63.4 ± 10.1 years), gender (male 48.4% vs. 62.5%), the prevalence of diabetes (25.8% vs. 45.6%), 25-hydroxyvitamin D (16.4 ± 9.0 vs. 21.7 ± 2.1 ng/ml), phosphorus, intact parathyroid hormone, creatinine (1.63 ± 0.38 vs. 1.75 ± 0.45 mg/dL), glomerular filtration rate (42.3 ± 10.9 vs. 40.3 ± 11.0 ml/min/1.73m2) and cystatin C (1.80 ± 0.55 vs. 1.89 ± 0.49 mg/dL) between patients taking omega-3 fatty acids and patients not taking omega-3 fatty acids. group was 1.823 (CI 95%: 0.928-3.579, p = 0.081) and in the 10-30 mg/ml group was 0.944 (CI 0.495-1.801, p = 0.861).

Conclusions: We showed that higher serum phosphorus at the initial visit predicted more rapid progression of CKD. Further studies are required to determine the benefits of phosphorus lowering in patients with CKD not on dialysis.

MP224 COMPARISON OF ACTIVE VITAMIN D LEVELS ACCORDING TO TAKING OMEGA-3 FATTY ACID IN PATIENTS WITH CHRONIC KIDNEY DISEASE
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Introduction and Aims: The level of 1, 25-dihydroxyvitamin D decreases according to decrease of activity of 1α-hydroxylase caused by reduced renal function in chronic kidney disease (CKD). Recent report showed that administration of omega-3 fatty acids increased 1, 25-dihydroxyvitamin D levels in dialysis patients. The purpose of this study is to evaluate whether administration of omega-3 fatty acids increase 1, 25-dihydroxyvitamin D levels in patients with CKD.

Methods: We retrospectively analyzed data of CKD patients who have checked 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D simultaneously from March 2009 to March 2013. We enrolled patients aged between 20 and 80 years and excluded CKD patients with stage 1, 2.

Results: The percentage of patients with 25-hydroxyvitamin D levels < 20 ng/ml was 73% and the percentage of patients with 1,25-dihydroxyvitamin D levels < 25 pg/ml was 15.9%. Patients taking omega-3 fatty acids were 32 cases (CKD stage 3 : 81.3%). There was no significant difference of age (59.8 ± 12.7 vs. 63.4 ± 10.1 years), gender (male 48.4% vs. 62.5%), the prevalence of diabetes (25.8% vs. 45.6%), 25-hydroxyvitamin D (16.4 ± 9.0 vs. 21.7 ± 2.1 ng/ml), phosphorus, intact parathyroid hormone, creatinine (1.63 ± 0.38 vs. 1.75 ± 0.45 mg/dL), glomerular filtration rate (42.3 ± 10.9 vs. 40.3 ± 11.0 ml/min/1.73m2) and cystatin C (1.80 ± 0.55 vs. 1.89 ± 0.49 mg/dL) between patients taking omega-3 fatty acids and patients not taking omega-3 fatty acids. group was 1.823 (CI 95%: 0.928-3.579, p = 0.081) and in the 10-30 mg/ml group was 0.944 (CI 0.495-1.801, p = 0.861).

Conclusions: Most patients with CKD stage 3 and 4 had vitamin D insufficiency but their active vitamin D levels were not lower than normal levels. Omega-3 fatty acids supplementation may involve with vitamin D activation and anemia prevention in CKD patients and further prospective studies are necessary to confirm the effectiveness of omega-3 fatty acids.

MP225 FAT MASS AS AN AGGRAVATING FACTOR FOR REDUCED BONE MINERAL DENSITY (BMD) IN RENAL TRANSPLANT RECIPIENTS
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Introduction and Aims: Low bone mineral density (BMD), a frequent finding after renal transplantation, may be ascribed to type and dosage of immunosuppression, persistence or de novo CKD-MBD, disturbances in phosphate homeostasis and appropriately high levels of PFG-23, presence of microalbuminuria and Vitamin D deficiency. A high prevalence of overweight and obesity has been frequently found after renal transplantation. Although a higher body weight or body mass index (BMI) has been traditionally associated with higher BMD in the general population, it has been suggested more recently that fat mass may exert a detrimental effect on BMD, possibly mediated through leptin. We aimed to evaluate the impact of obesity and fat mass in non-diabetic renal transplant recipients (RTR).

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Methods: A hundred (100) nondiabetics RTR (62M/38F, 42.4 ±10.5 years old) with serum creatinine <2.0 mg/dL and at least 6 months of transplantation met eligibility for this cross sectional study. All RTR were subjected to an anthropometric evaluation and body composition assessment through bioelectrical impedance. A fasting blood sample was drawn for serum biochemical and hormonal determinations, bone mineral density (BMD) was assessed by dual-energy x-ray absorptiometry (DEXA) and a spot urine sample was collected to determine albuminuria. Associations were examined in a multiple linear regression analysis.

Results: Sixty (60%) of RTR evaluated up to 165 months after transplantation presented low BMD. We also observed overweight (BMI > 25 kg/m2) in 59% of cases and a significant mean weight gain after transplantation of 5.1 kg. An inadequate distribution of body fat was evidenced in 50% of males and 58% of females. Hypovitaminosis D was observed in 65% of patients, with levels indicating Insufficiency [25(OH)D < 30 ng/ml] in 53% and Deficiency [25(OH)D < 15 ng/ml] in 12%. The univariate linear regression showed significant associations (p=0.001) between female gender, levels of 25(OH)D, weight gain, BMI, body fat, lean mass and serum leptin levels and both lumbar spine and femoral neck BMD. Finally, the multivariate linear regression analysis showed that serum leptin levels and BMI were the only significant (p=0.01) variables remaining in the model predictive of low BMD in the present sample.

Conclusions: The present study showed a high percentage of overweight, body fat and weight gain after renal transplantation combined to a high level of BMD and hypovitaminosis D. Serum leptin levels and BMI were considered the only independent risk factors for low BMD in these patients, suggesting that excessive fat mass may have an unfavorable impact on bone mass in RTR.

**MP227**

**PILL BURDEN AND ELEMENTAL CALCIUM INTAKE ASSOCIATED WITH CALCIUM CARBONATE AND LANTHANUM CARBONATE MONOTHERAPY**

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Introduction and Aims: Hyperphosphataemia can be managed with phosphate (P) binders, which can be calcium-based, such as calcium carbonate (CC), or non-calcium-based, such as lanthanum carbonate (LC). Calcium-based P binders increase calcium load and may be associated with episodes of hypercalcaemia, increased vascular calcification and adynamic bone disease. The aims of this study were to compare the pill burden associated with CC and LC monotherapy, and to determine the elemental calcium intake associated with CC and LC monotherapy.

Methods: We conducted a post hoc analysis using data from a phase 4 study of patients with end-stage renal disease (ESRD) and hyperphosphatemia in a real-world clinical practice setting. The study design comprised a 1-week observation period in which patients remained on their existing P binder, a 12-week LC monotherapy titration phase (starting dose: 1500 mg/day; planned maximum dose: 3750 mg/day) and a 4-week LC maintenance period. Serum P level and daily P binder dose were assessed at baseline for patients treated with CC and after 16 weeks of LC monotherapy.

Results: At baseline, 276 patients were receiving treatment with CC monotherapy, 204 (74%) of whom were receiving LC at 16 weeks post-baseline. Mean P binder doses, serum P levels and elemental calcium intake, overall and by previous CC dose group, are shown in the table below. The overall tablet burden was 8 CC tablets versus 3 LC tablets. The recommended maximum daily intake of elemental calcium from calcium-based P binders is 1.5 g; the mean daily intake of elemental calcium from CC was 1.5 ± 4 in approximately 75% of patients. The recommended maximum daily intake of elemental calcium from all sources is 2.0 g; the mean daily intake of elemental calcium based on calcium content of their CC binder alone was 2.2 ± 0.9 g in approximately 47% of patients.

Conclusions: The lower pill burden with LC (3 tablets compared with 8 CC tablets) may improve adherence and thus outcome in patients with ESRD. The mean daily intake of elemental calcium from CC P binders was 2.1 ± 0.5 g in approximately 75% of patients, which may have implications regarding vascular calcification.
Hypovitaminosis D is well documented in patients with chronic kidney disease (CKD) and has been associated with poor outcome even in the earlier stages of the disease. This study aimed to evaluate the prevalence of hypovitaminosis D in nondialyzed patients with CKD and to investigate the risk factors for hypovitaminosis D in Table 1. In 7 out of 11 patients (64%) RLS was diagnosed. The mean rating scale of the IRSSG score was 25.7 ± 3.3 prior to operation. Two patients (18%) remained with RLS symptoms after PTx (p = 0.03). In these patients the rating scale of the IRSSG score dropped from severe to moderate, despite the unchanged iron status. PLM was above normal range in 4 of 7 patients with RLS (57%). PLM index (PLM events/hour of sleep) reduced from 16.3 (3.3, 41.0) to 3.5 (0.2, 1.4), although did not reach statistical significance (p = 0.102). There was a positive correlation between baseline PLMI and serum phosphate levels (Figure 1).

Conclusions: Parathyroidectomy can alleviate RLS in patients under hemodialysis. Further studies are necessary to elucidate the exact mechanism on whether the PTx can improve RLS, and if this effect is unequivocal and independent of phosphate control.

Hypovitaminosis D is well documented in patients with chronic kidney disease (CKD) and has been associated with poor outcome even in the earlier stages of the disease. This study aimed to evaluate the prevalence of hypovitaminosis D in nondialyzed patients with CKD and to investigate the risk factors for hypovitaminosis D.

Methods: This cross-sectional study included 270 patients with CKD at stages 2 to 5 (51.9% male; age: 64.1 ± 16.5 year, estimated glomerular filtration rate (GFR) 30.8 ± 14.1 mL/minute, 32.5% diabetics). Serum 25-hydroxyvitamin D (25-(OH)D) was measured by chemiluminescent microparticle immunoassay, and analyzed the clinical and laboratory variables related to patients with adequate levels of 25-(OH)D (> 30ng/ml) and hypovitaminosis D (≤30ng/ml). The following laboratory parameters were measured: calcium (Ca), phosphorus (P) and intact parathyroid hormone (iPTH).

Results: Hypovitaminosis D was observed in 56.7% of patients, 51.5% had insufficiency (15 to 30ng/ml) and 5.2% deficiency (<15ng/ml). The risk factors for hypovitaminosis D were female (odds ratio: 1.77; 95% CI: 1.05 to 2.96; p = 0.030), diabetes (odds ratio: 3.31; 95% CI: 1.84 to 5.96; p < 0.001), GFR < 30mL/minute (odds ratio: 1.75; 95% CI: 1.04 to 2.93; p = 0.033). The table below shows the comparative analysis of the groups.

Conclusions: Parathyroidectomy can alleviate RLS in patients under hemodialysis. Further studies are necessary to elucidate the exact mechanism on whether the PTx can improve RLS, and if this effect is unequivocal and independent of phosphate control.

Hypovitaminosis D is well documented in patients with chronic kidney disease (CKD) and has been associated with poor outcome even in the earlier stages of the disease. This study aimed to evaluate the prevalence of hypovitaminosis D in nondialyzed patients with CKD and to investigate the risk factors for hypovitaminosis D.

Methods: This cross-sectional study included 270 patients with CKD at stages 2 to 5 (51.9% male; age: 64.1 ± 16.5 year, estimated glomerular filtration rate (GFR) 30.8 ± 14.1 mL/minute, 32.5% diabetics). Serum 25-hydroxyvitamin D (25-(OH)D) was measured by chemiluminescent microparticle immunoassay, and analyzed the clinical and laboratory variables related to patients with adequate levels of 25-(OH)D (> 30ng/ml) and hypovitaminosis D (≤30ng/ml). The following laboratory parameters were measured: calcium (Ca), phosphorus (P) and intact parathyroid hormone (iPTH).

Results: Hypovitaminosis D was observed in 56.7% of patients, 51.5% had insufficiency (15 to 30ng/ml) and 5.2% deficiency (<15ng/ml). The risk factors for hypovitaminosis D were female (odds ratio: 1.77; 95% CI: 1.05 to 2.96; p = 0.030), diabetes (odds ratio: 3.31; 95% CI: 1.84 to 5.96; p < 0.001), GFR < 30mL/minute (odds ratio: 1.75; 95% CI: 1.04 to 2.93; p = 0.033). The table below shows the comparative analysis of the groups.

Conclusions: Parathyroidectomy can alleviate RLS in patients under hemodialysis. Further studies are necessary to elucidate the exact mechanism on whether the PTx can improve RLS, and if this effect is unequivocal and independent of phosphate control.
10 classes of images. We used same color for same class number both ClbSS and ClaSS images. If color classes are in same structure of face (on cheek, forehead, etc), they may be combined.

**Results:**
We have very important results on deformed faces photos in SS. Figure 3, Column 1: photos of patients before SS (raw images), column 2: classified photos of column 1, column 3: classified photos of patients after SS. Figure 5. ‘Hourglass’ is conformity of ‘Hourglass’ form for all ClaSS curved face.

**Conclusions:**
Image processing plays very important role in clinical practices and biomedical researches. SS is a kidney disease and derived from inside of the body but its effects are appearance outside of human body, such as head, face, skull deformations. These symptoms can be put forward by using Image Classification for SS. Moreover, shape of ‘hourglass’ can be an index for SS and this is very specific for SS. ‘Hourglass’ can be an indicator for grading SS. Finally, ‘hourglass’ should be carefully evaluated in Saglker syndrome.

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**MP232 PARATHYROID HORMONE 1–84 EQUIVALENT VALUE TO INTACT PTH**

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**Introduction and Aims:** Hyperparathyroidism is one of the major complications of chronic kidney disease (CKD) and PTH measurement is required to make a precise diagnosis. PTH 1–84 assay is introduced recently. However, current clinical guideline recommends management of hyperparathyroidism in CKD according to intact PTH (iPTH) level. In this study, we estimated PTH 1–84 equivalent to iPTH value.

**Methods:** PTH 1–84 and iPTH were simultaneously measured in CKD patients. The predicted value of PTH 1–84 for iPTH was estimated using linear regression analysis.

**Results:** Ninety-four pairs of tests (M: 91) were conducted in 69 patients (M: 66). The median age was 66(34–83). Sixty-one percent diabetic, 84% was hypertensive, and 71.3% was dialysis patients. Linear regression analysis showed that as iPTH increased by 10 pg/mL, PTH 1–84 increased by 5.8 pg/mL (95% CI: 5.6–6.0) (Figure). PTH 1–84 equivalent to 150 and 300 pg/mL iPTH was 82.0 (95% CI: 77.4–86.7) and 169.2 pg/mL (95% CI: 164.0–174.4) respectively.

**Conclusions:** The PTH 1–84 equivalent to iPTH was estimated as -5.13 + 0.58 x iPTH (pg/mL).

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**MP233 ASSOCIATION OF SURROGATE ENDPOINTS (SERUM PARATHYROID HORMONE, CALCIUM AND PHOSPHORUS) WITH MORTALITY IN CHRONIC KIDNEY DISEASE TRIALS: A META-ANALYSIS**

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**Introduction and Aims:** In observational studies, elevated levels of serum phosphorus, parathyroid hormone and calcium are associated with vascular calcification, cardiovascular events and mortality. Intervention trials to manage perturbed mineral metabolism in chronic kidney disease commonly use surrogate endpoints to evaluate drug efficacy (serum parathyroid hormone and phosphorus). We evaluate whether treatment-related changes in surrogate endpoints of mineral and bone disorder are associated with risk of mortality in individuals with chronic kidney disease.
**Methods:** We searched Medline, Embase and Cochrane databases in September 2010. Randomised trials that reported treatment effects on serum phosphorus, parathyroid hormone or calcium levels in individuals with chronic kidney disease and total or cardiovascular deaths were eligible. For each study, we computed the log ratio of the mean for the surrogate endpoint at end of the treatment between the intervention and control arms (represented in the horizontal axes of the figure) and the log risk ratio of mortality endpoint (vertical axes) as well as the 95% confidence ellipses for the estimates. Thus, studies in the lower right-hand quadrant of the plot showed concordance in favour of the intervention on both the surrogate endpoint and mortality. We then summarised the association between treatment effects on surrogate endpoints and mortality by computing the correlation using a Bayesian approach with uninformative priors.

**Results:** Overall, there were poor correlations between treatment effects on surrogate endpoints and risks of mortality (figure). Correlations between surrogate and mortality endpoints and their 95% credible intervals are shown in the table below.

**Conclusions:** The lack of association between surrogate biomarkers and mortality risks in randomised trials suggest that treatment effects captured by changes in serum phosphorus, calcium or parathyroid hormone are weak signals for drug evaluation in the setting of chronic kidney disease.

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**MP234**

**RISK OF FRACTURE IN CHRONIC KIDNEY DISEASE**

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**Introduction and Aims:** Chronic kidney disease (CKD) has many complications. One of these is renal bone disease. In those on renal replacement therapy (RRT) there is an increase in the risk of fracture. The evidence regarding those with less advanced CKD is not so clear cut. We aimed to identify the risk of suffering a hip fracture in those with CKD and compare this to those with normal renal function, to ascertain whether the effect of renal bone disease is a biochemical/sub-clinical one in those with less advanced CKD.

**Methods:** The GLOMMS-II cohort contained all individuals with a low eGFR (<60 ml/min/1.73m²) measured in the Grampian health board region in 2003; all those with raised PCR and ACR; all those receiving RRT; and a 20,000 sample of those with only normal eGFR measurements in 2003. Data linkage to hospital episode statistics from the index date to 30th June 2009 for hip fractures and related procedures allowed ascertainment of hip fracture rates. Incidence rate ratios for first hip fracture post-index and the association with severity of CKD versus normal renal function were calculated, with adjustment for age and sex.

**Results:** For this analysis there were 19852 individuals with normal renal function (47.1% males, median age 53 years) and 19523 with CKD (35.2% male, median age 76 years). There were 1078 individuals who sustained at least one hip fracture during follow-up. The rate of first-observed fracture during follow-up, and both unadjusted and age-sex adjusted rate ratios are shown in the table below.

**Conclusions:** As GLOMMS-II was a population based cohort with complete capture for a single health authority region, with complete follow-up for all still resident in Scotland, our findings are relevant to others practising elsewhere in Europe. Those with CKD in the GLOMMS-II cohort were older and more likely to be female, which are common risk factors for fracture. Those with CKD had higher rates of hip fracture than those with normal renal function, this was partially confounded by the age and sex of those with CKD. However after correction for age and sex there still appeared to be a statistically significant increase in the risk of fractures even amongst those with stage 3a CKD. Even those with less advanced CKD should be considered at increased risk of fractures. Future trials of fracture prevention should investigate how best to minimise this risk.

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**Conclusions:** The lack of association between surrogate biomarkers and mortality risks in randomised trials suggest that treatment effects captured by changes in serum phosphorus, calcium or parathyroid hormone are weak signals for drug evaluation in the setting of chronic kidney disease.