**CKD BONE DISEASE**

**MP201**  
**MAGNESIUM PROMOTES OSTEGENESIS 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 with 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.

<table>
<thead>
<tr>
<th>Table 1 - Levels of selected osteogenic markers</th>
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<tr>
<td>UC</td>
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</tr>
<tr>
<td>Runx2 (x-fold expression)</td>
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<tr>
<td>Osteocalcin (x-fold expression)</td>
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<td>ALP activity (AU/µg protein)</td>
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</table>

**MP202**  
**TWO PHOSPHATURIC HORMONES PREDICT THE PROGRESSION OF CKD IN ANEMIA PATIENTS WITH Ckd**

Chikako Nakano1, Takayuki Hamano1, Naohiko Fujii2, Isao Matusi1, Satoshi Miki1, Kodo Tomid1, Daisuke Mori1, Yasuo Kusunoki1, Akhiro Shimomura1, Yoshitsugu Obi1, Terumasa Hayashi4, Hiromi Rakugi1, Chikako Nakano1, Takayuki Hamano1, Naohiko Fujii2, Isao Matusi1, Satoshi Miki1, Kodo Tomid1, Daisuke Mori1, Yasuo Kusunoki1, Akhiro Shimomura1, Yoshitsugu Obi1, Terumasa Hayashi4, Hiromi Rakugi1, Yolanda Almaden4 and Juan R Muñoz-Castañeda1

1.Aarhus University Hospital, Aarhus N, Denmark, 2.Aarhus University Hospital, Aarhus, Denmark, 3.Hospital unit West, Herning, Denmark

**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 (hb) 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 738 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 at 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 S, CIJN2012), 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.

<table>
<thead>
<tr>
<th>MP203 vBMD and low-trauma fracture</th>
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<tbody>
<tr>
<td>Region</td>
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<tr>
<td>--------</td>
</tr>
<tr>
<td>Lumbar spine</td>
</tr>
<tr>
<td>Total hip</td>
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<tr>
<td>Femoral neck</td>
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</table>
THE WHOLE 12 EXONS OF GNAS1 GENE AND THE GENES FOR HEREDITARY OSTEODISTROPHIAS (HO) IN SAGLIKER SYNDROME (SS), COMBINATION-COMPELLUSION OF HEREDITARY OSTEODISTROPHIAS AND CHRONIC KIDNEY DISEASES (CKD)?

Yahya Saglik1, Osman Demirhan2, Ismail Yildiz2, Nuray Paylar1, Nihal Inandiklioglu2, Eyul Akba2 and Erdal Tunc2
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Introduction and Aims: Sagliker 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 conducted clinical and biological studies including screening for mutations in the 13 exons of GNAS1 gene in 23 patients (mean age: 26.5±12.0; 17 males, 6 females) 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 bone densitometry. DNA isolation was performed from blood samples of the subjects and mutations regions were amplified by Polymerase Chain Reaction (PCR). The patients were screened for the gene encoding the subunit of GNAS1 were designed using Gene Runner Programme.

Results: GNAS1 gene lesions were found in 9/23 patients (39%). Thirteen different missense and nonsense mutations were detected in exons 1, 4, 5, 10 and some intronic polymorphism (in exons 3, 6, 10 and 12), and were not detectable in other exons. In seven patients, a different missense mutation in the 284 codon of exon 1 showed in P1. P5 had a heterozygote missense mutation in the 786 codon of exon 4. P12, P13, P15 and P23 showed an missense mutation in codons 750, 747 and 769 of exon 4 respectively. P20 showed a single base substitution in codon 885 of exon 4. No genetic alterations were found in fourteen patients with SS as the only clinical manifestation.

Conclusions: These results expand the spectrum of GNAS1 missense mutations associated with this disorder, and are consistent with an insufficiency of GNAS1 playing a role in the clinical phenotype of loss of function mutations and with a functional GNAS1 allele having a predominant role in preventing the hormonal resistance. Further investigations into mutation effects and the regulation and function of the multiple transcripts of the all GNAS1 locus will be required to understand the genotypic complexity and phenotypic variability associated with mutations at this gene. And lastly SS might be a combination-compulsion of HO and CKD~? This is the first marginal report in the medical literature so far for the etiology in SS.
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 (n=1)</th>
<th>Control (n=30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sost, pmol/l</td>
<td>59±16</td>
<td>28±10</td>
<td>0.001</td>
</tr>
<tr>
<td>OPG, pg/ml</td>
<td>5.3±3</td>
<td>0.1±0.2</td>
<td>0.001</td>
</tr>
<tr>
<td>RANKL, mcg/ml</td>
<td>4.7±1</td>
<td>0±0.5</td>
<td>0.001</td>
</tr>
<tr>
<td>IL-1, pg/ml</td>
<td>0.2±0.5</td>
<td>0.01±0.03</td>
<td>0.001</td>
</tr>
<tr>
<td>IL-6, pg/ml</td>
<td>12±3</td>
<td>0.3±0.3</td>
<td>0.001</td>
</tr>
<tr>
<td>IL-10, pg/ml</td>
<td>9.5±3.9</td>
<td>3.3±1.3</td>
<td>0.001</td>
</tr>
<tr>
<td>TNFα, pg/ml</td>
<td>1.1±1</td>
<td>3±2</td>
<td>0.001</td>
</tr>
<tr>
<td>PTH, pg/ml</td>
<td>34±3.6</td>
<td>34±15</td>
<td>0.001</td>
</tr>
<tr>
<td>Ca, mg/dl</td>
<td>9.8±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±8</td>
<td>0.001</td>
</tr>
<tr>
<td>1,25D, pg/ml</td>
<td>11.8±15</td>
<td>56±12</td>
<td>0.001</td>
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</table>

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 268 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 (Teckmedical) 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 Hoxhaanson criteria. The cross-sectional analysis demonstrated a direct association at baseline between sclerostin levels 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. This data 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.

MP206 INFLAMMATION MAY INDUCE AN OSTEOCLASTOGENIC PHENOTYPE IN PERIPHERAL MONONUCLEAR CELLS (PBMC) OF CHRONIC KIDNEY DISEASE (CKD) PATIENTS

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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) cell functions. In pathological conditions, immune cells and inflammatory cytokines belonging to tumor necrosis factor family, 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 positive (TRAP+) multinucleated cells containing 3 or more nuclei. The presence of circulating osteoclast precursors (CD14+/CD16+) and the LIGHT and RANKL expression through miR modulation. As known targets of miR-30b, miR-133a and miR-143 are Runx2 and Osterix, our analyses provide a potential mechanistic explanation of the observed up-regulation of these master switches in the course of VC.

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Introduction and Aims: Vascular calcification (VC) is prevalent in patients suffering from chronic kidney disease (CKD). Factors promoting VC include abnormalities in mineral and bone metabolism, particularly high phosphate levels. Inorganic phosphate (Pi) is a classical inducer of in vitro VC. Previously, we demonstrated that magnesium (Mg) was able to prevent VC in human aortic vascular smooth muscle cells (HAVSMC). As microRNAs (miR) are known modulators of gene expression in many different processes and diseases, we aimed at investigating the role of selective miR in this protective effect of Mg on VC.

Methods: HAVSMC were obtained from aortas of 3 donors (ethical procedure approval # 2009/19) and cultured in the presence of 3 mM Pi with or without 2 mM Mg chloride. miR-29b, -30b, -125b, -133a, -143, -204 were extrapolated from the literature as potential regulators in the VC process. RNA from donor HAVSMC was extracted after 4h, 24h, day 3, day 7, and day 10, and miR levels in different conditions were assessed by TaqMan® qPCR.

Results: miR-30b -133a and -143 were down-regulated during the time course in the presence of Pi, whereas the addition of Mg restored (miR-30b) or improved (miR-133a, miR-143) expression. miR-29b and miR-204 expressions were slightly but not significantly changed in our experimental setup. miR-125b levels were not modified over the whole time course at any condition.

Conclusion: Our data demonstrated that miR-30b, miR-133a and miR-143 expressions are negatively regulated by Pi and restored by Mg. Thus, Mg’s beneficial effect on Pi-induced VC in HAVSMC seems to involve an active influence on gene expression through miR modulation. As known targets of miR-30b, miR-133a and miR-143 are Runx2 and Osterix, our analyses provide a potential mechanistic explanation of the observed up-regulation of these master switches in the course of VC.

The modulation of the targets as well as the in vivo relevance of these phenomena remains to be shown in future studies which will undoubtedly help to understand the protective effect(s) of Mg on VC.

MP209 RETROSPECTIVE REVIEW OF BONE DENSITY SCANS IN DIFFERENT STAGES OF CHRONIC KIDNEY DISEASE

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Introduction and Aims: A substantial population of patients with chronic kidney disease (CKD) also experience reductions in bone mineral density which can result in bone fractures. Our renal program undertook a retrospective chart review of all patients who underwent a baseline dual-energy X-ray absorptiometry (DXA) scan in our multidisciplinary CKD clinic from Jan 2001 to Jan 2010. The purpose of the study was to determine if there was a preferential site of bone loss in CKD patients across different disease stages.

Methods: A total of 410 patients were included in the dataset. Measures included demographics, baseline creatinine, glomerular filtration rate (eGFR) in ml/min as per
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.

Results: We found a significant decline in median 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-subjects analysis (X2 (3) = 6.42, p=.09, Cramer’s V = .13, 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 scans 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.

MP210 SEVERE HYPOCALCEMIA PERSISTS IN THE YEAR AFTER PARATHYROIDECTOMY: RESULTS FROM THE DIALYSIS OUTCOMES AND PRACTICE PATTERNS STUDY

Francesca Tentori1, Lindsay Zepel1, Leah Comment1,2, Takashi Akiba3, Juergen Bommer4, Masatumi Fukagawa5, David A Goodkin1, Stefan H Jacobson6, Kathleen Claes1

Introduction and Aims: In recent years, medical therapies (vitamin D analogs; calcimimetics) have led to a decline in surgical parathyroidectomy (PTX) among hemodialysis patients. However, this procedure is uncommon in some DOPPS regions, ranging from 2.0 (Japan) to 14.3 (Canada) PTX per 1000 patient years. Severe hypocalcemia in the immediate post-operative period is a well-known complication of PTX, but the extent to which it persists is not well understood.

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 PTH, calcium, and phosphorus were examined over the 3 months prior to and 12 months after PTX.

Results: Median PTH 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 (60 to 73%). Cinacalcet use decreased from 23% before surgery to < 10% in the month after surgery. Mean peak PTH levels decreased from 4.1 mg/dl in the month prior to surgery to 4.1 mg/dl in the month after surgery, and ranged from 5.5 to 5.7 mg/dl in months 4 to 12 after surgery.

Conclusions: PTH levels remained inappropriately high in a substantial number of incident renal transplant recipients. In various experimental models and clinical studies, PTH has been shown to repress the expression of sclerostin, an antagonist of Wnt/beta-catenin signaling. Wnt/beta-catenin signaling is of paramount importance in the regulation of bone homeostasis. Data on the crosstalk between PTH and Wnt/ beta-catenin signaling in renal transplant recipients is lacking.

Methods: We monitored parameters of mineral metabolism, bone biomarkers and circulating sclerostin (ELISA, Tecomedical, ng/ml) levels (a) in incident renal transplant recipients (n=64, 40 male, age 51 ± 11 y) immediately before transplantation (baseline) and at day 7, month 3 and 12 post-transplantation, and (b) in patients with severe persistent hyperparathyroidism (n=23, 10 male, age 53 ± 11 y) before and after parathyroidectomy. Results were compared with data obtained in healthy volunteers (n=21, 5 male, age 41 ± 12 y) and CKD patients (n=50) matched (1:1) for age and eGFR.

Results: Sclerostin serum levels decreased by 61.7% (54.6-68.5) between baseline (1.22 ng/ml [0.79-1.48]) and month 3 (0.42 ng/ml [0.34-0.58]), to increase again by 24.4% (2.0-4.08) between month 3 and 12. Higher age and lower PTH independently associated with higher sclerostin levels, both at baseline and at month 12. Sclerostin levels at month 12 (0.53 ng/ml [0.41-0.72]) were lower than in CKD counterparts (0.63 ng/ml [0.48-0.86]). Sclerostin levels increased following parathyroidectomy (post: 0.49 ng/ml [0.32-0.57] vs. pre: 0.32 ng/ml [0.26-0.42]). The time course changes of bone biomarkers after parathyroidectomy suggest that bone resorption normalizes earlier than bone formation.

Conclusions: Sclerostin levels rapidly decrease after renal transplantation, with age and PTH being major determinants. Sclerostin levels increase towards normal in patients with persistent hyperparathyroidism following PTX. Our data confirm crosstalk between PTH and Wnt/beta-catenin signaling.

MP212 EXPERIENCE OF PARATHYROIDECTOMY FOR MORE THAN 3000 PATIENTS WITH ADVANCED CONCURRENT HYPERPARATHYROIDISM IN A SINGLE CENTER

Yoshitomo Tominaiga1, Takahisa Hiramitsu1, Takuya Yamamoto1, and Makoto Tsubota1

Nagoya Second Red Cross Hospital, Nagoya, Japan

Introduction and Aims: Secondary hyperparathyroidism (SHPT) due to chronic kidney disease (CKD) is one of serious complications for continuous hemodialysis (HD) patients. Surgical indications of parathyroidectomy (PTXs) might be influenced by medical treatment. We evaluated these issues in patients who underwent PTXs in our huge series.

Methods: Between July 1973 and June 2013, total 3000 patients underwent PTXs for advanced SHPT in our center. The period was divided into 5 Eras based on medical treatment as following Era 1: 1973-1981, ERA 2: 1982-1990, ERA 3: 1991-2000, ERA 4: 2001-2008, and ERA 5: 2009-2013. Cinacalcet+IV DRA In Era 1, 2 and 3 bone disease and symptoms were major factors for surgical indications. In Era 4 and 5, size of parathyroid glands and to prevent ectopic calcification were significant factors to decide PTX. In Era 1 subtotal PTX and in Era 2,3,4,5, total PTXs with forearm autograft was performed. The patient’s profiles, laboratory findings at PTX and after PTX and surgical outcomes were evaluated.

Results: 1. Age at PTXs was gradually elder in Era 1,2,3 and then that was stable, 2. Duration between beginning of HD and PTXs also prolonged in Era 1,2,3,4,5. At PTX serum Ca and P levels were stable however ALP and PTH levels gradually decreased in whole periods. Overall in 4.9% patients fewer than 4 glands, in 77.4% patients 4 glands

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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.6 After PTx serum Ca,P 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, i.e. 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.

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 reflected 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, 25OH vitamin D, PTH, FGF-23, sclerostin and BAP was taken immediately before initial operation.5, Total glandular weight and weight of the largest gland has gradually decreased in all Era.6 After PTx serum Ca,P 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, i.e. husky voice were negligible.9, 10 years and 20 years patient's survivals after PTx were 83.1% and 61.9%.

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)**

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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 active vitamin D treatment. However, parathyroidectomy (PTx) is performed in patients with severe SHPT refractory to CH. In this study, we investigated effects of preoperative CH treatment on operative course and pathological findings of resected PTG in PTx.

Methods: 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.

Results: In preoperative period, 33 patients had CH therapy. There was no significant difference in intact-PTH, the number of resected PTGs, operative time between patients with or without CH (Table). However, total PTGs volume and the largest PTGs volume were significantly lower, and more adhesions of PTGs against surrounding tissues were significantly greater in patients with CH as compared with patients without CH. In addition, cystic changes or hemorrhagic necrosis of resected PTGs were observed more frequently in patients with CH.

Conclusions: Preoperative CH treatment might introduce pathological changes in resected PTGs in PTx for severe SHPT.

**MP215**

**COLESTILAN IN CHRONIC KIDNEY DISEASE STAGE 5 DIALYSIS PATIENTS WITH HYPERPHOSPHATAEMIA: A COMBINED SAFETY ANALYSIS PROFILE**

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Introduction and Aims: Colestilan (COL) is a novel, non-absorbed bile acid sequestrant that has been shown to be an effective phosphate binder with additional potential benefits in hyperlipidaemic, hyperuricemic and hyperglycaemic patients. Here we show a combined safety analysis profile of COL in 12 phase II and III clinical trials.

Methods: All patients randomised presented with Chronic Kidney Disease Stage 5D with hyperphosphataemia. 1363 pts received colestilan alone, 47 pts colestilan 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. 57% were male. Patients were exposed to 3 to 15g/day COL for up to one year.

Results: Overall 7.5% pts treated with COL reported one or more Treatment Emergent Adverse Events (TEAE), 9.5% pts treated with calcium binders and 9.5% treated with SEV. Most frequent TEAEs for both COL and SEV pts were GI disorders - nausea, vomiting, diarrhoea, dyspepsia, constipation and abdominal pain. Incidence was 53.8% in SEV pts and 45.1% COL pts. For COL, in terms of severity, 26% were mild, 36.9% were moderate and 12.2% severe, as opposed to 32.0%, 46.2% and 16.0% for SEV. In terms of Treatment-Related TEAEs, the highest incidence reported was GI disorders and a dose-dependent increase was seen with COL (from 11.5% with 3g/day to 33.7% with 15g/day). Incidence of GI treatment-related TEAEs of SEV and COL was the same - 27.8% for both groups. In terms of mortality, 2.2% pts died treated with COL and 3.0% treated with SEV.

Conclusions: The safety profile of COL is as expected for a nonabsorbed anion exchange resin and is essentially similar to that of SEV.

**MP216**

**THE EFFECT OF GH TREATMENT COMBINED WITH EXERCISE ON THE EPINEPHALY GROWTH PLATE OF YOUNG CKD RATS**

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Introduction and Aims: Linear growth retardation in children with CKD has been ascribed to growth hormone (GH) insensitivity. This resistance state has been
attributed 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 bone and epiphyseal growth plate (EPP) GH receptor signaling. We have also recently shown that endurance exercise improves EGP architecture and IGF-I content in a rat CKD model. Reombinant human growth hormone (rhGH) 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 were sham operated (C group). The CKD group was further divided into 3 groups: 1. (CKD)- receiving daily saline. 2. (CKDgh) - receiving daily rhGH (5mg/kg SC). 3. (CKDgh + run) - receiving rhGH plus 30 minutes of treadmill exercise at 17 m/min in 15° elevation. 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 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, rhGH corrected this deacre to the levels of C and in CKDgh + run there was significant increase compared to C.

**Conclusions:** Longitudinal growth was not increased following rhGH 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 combined GH-exercise intervention showed potential beneficial effects on markers of differentiation towards more mature hypertrophic chondrocytes, which are responsible for normal growth through endochondral ossification.

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**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:** Accordingly to the expression of osteonectin, the time course of calcium formation may be worth further investigation.

**Conclusions:** To prevent the development of VC in animal models of CKD. However, the possibility of harmful effects of exogenous administration of PPI on bone requires further investigation. To this end, we examined by histomorphometry the bone of CKD mice after intraperitoneal PPI 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 PPI 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 PPI dose (OV/BV, O.Th and O.SB/BS) and, for one parameter measured, to high PPI dose (O.Th), compared to placebo-treated CKD mice. Treatment with PPI did not modify any other structural parameters. Mineral apportion rate, other parameters of bone formation and resorption were not significantly different among the treated animal groups or control groups.

**Conclusions:** In conclusion, PPI does not appear to be deleterious to bone tissue in apoE/- mice with CKD, although a possible stimulatory PPI effect on osteoid formation may be worth further investigation.
Introduction and Aims: Post TX HPSH can be considered as result, at least partly, from decreased expression of CaSR and VdD- (VDR) receptors on parathyroids. 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: Out 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 mg/kg/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 for 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 deterministic factors 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 ng/ml, 2) insufficient 25(OH)D – i.e. between 10 ng/ml and 29 ng/ml and 3) deficient 25(OH)D – i.e. <10 ng/ml.

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 ng/ml group (HR) for death in the group with vitamin D levels <10 ng/ml was 2.572 (CI 95%: 1.337-4.984, 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 ng/ml group was 1.823 (CI 95%: 0.928-3.579, p = 0.081) and in the 10-30 ng/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 nonspecific marker for a poor health status, with less impact on mortality.

Compliance with ethical standards

Conflict of interest

None.

Table 1: Demographic data of the patients

<table>
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<th>Characteristic</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
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<td>Age (years)</td>
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<td>58.1 ± 12.3</td>
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<td>Gender (male)</td>
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<tr>
<td>Diabetes (%)</td>
<td>26.7%</td>
<td>25.8%</td>
<td>25.6%</td>
<td>25.9%</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>62.5%</td>
<td>64.3%</td>
<td>63.7%</td>
<td>62.8%</td>
</tr>
</tbody>
</table>

Introduction and Aims: The study was to investigate the circulating vitamin D metabolites after serial suberythema irradiation with a sun-simulating UV spectrum and the vitamin D activation by uric skin.

Methods: 22 ESKD patients (11 fem.; median age 51.5 [range 41-57] yrs.) were exposed wholebody to UV irradiation before starting dialysis treatment 3-times weekly for 14 months. The irradiation dose was individualized after UV testing of the skin for erythema.

Results: After 6 months there was a significant increase and normalization of all vitamin D metabolites: vitamin D3 500% (6 > 33 ng/ml), 25-hydroxyvitamin D3 150% (20 > 30 ng/ml), 1,25-dihydroxyvitamin D3 225% (25 > 35 pg/mL), 24,25-dihydroxyvitamin D3 225% (1.25 > 1.6 ng/ml), 25-hydroxyvitamin D3 continuously increasing, 1,25-dihydroxyvitamin D3 with mean eGFR was 33.0 ml/min/1.73m2. Percentages of history of cardiovascular disease, diabetes and hypertension were 26.7%, 37.1% and 90.7%. Mean eGFR was 33.0 ml/min/1.73m2. Patients in Group 4 had more frequently diabetes, hypertension, and lower eGFR and higher proteinuria. A total of 120 patients reached the composite endpoint of ESKD or reduction by half of eGFR during one year (88 patients reached ESKD, and 32 patients had a reduction by half of eGFR), for an overall incidence rate of 136.8/1000 patient-years. Higher serum phosphorus was associated with a higher risk for the composite endpoint for phosphorus levels Group2, Group3, and Group4 versus Group1, adjusted hazard ratio 1.32 (95%confidence interval 0.86 to 2.09), 1.14 (0.74 to 1.82), and 1.84 (1.27 to 2.84).

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.

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, gender and inappropriate high levels of FGF-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 > 25kg/m2) in 59% of cases and a significant median weight gain after transplantation of 5.1 kg. An inadequate distribution of body fat was evidenced in 50% of males and 6% 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 regressions showed significant associations (r=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<0.001) 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 risk of low 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.

**MP228 ASSOCIATION BETWEEN ALKALINE PHOSPHATASE AND TOTAL BONE MINERAL DENSITY IN CKD STAGE 5 PATIENTS**

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**Introduction and Aims** The altered bone and mineral metabolism in patients with chronic kidney disease (CKD) contributes to vascular calcification (VC). Recent prospective studies report on an inverse relationship between bone mineral density (BMD) and VC in CKD patients. Alkaline phosphatase (ALP) and bone specific ALP (BALP) are predictors of increased mortality in patients with CKD. BALP has shown higher sensitivity and specificity than total ALP in reflecting histological alterations in bone. However, associations between ALP, BALP and BMD in previous studies are inconsistent. The aim of this study was to evaluate the relation of total ALP and BALP with measurements of total BMD in CKD patients during 24 months.

**Methods** This observational prospective study followed 194 patients with CKD stage 5 (median age 57 years, 66% male, 32% diabetes mellitus, mean BMI 24.8 kg/m2) during their first 24 months on dialysis treatment. Serum total ALP and BALP (by routine and ELISA-techniques, respectively) and total BMD (by dual-energy X-ray absorptiometry) were measured at dialysis start and after 12 and 24 months. During the study period, the serum concentrations of ALP and BALP increased significantly (p<0.001), whereas BMD values remained stable.

**Conclusions** These results suggest that ALP and BALP are associated with total BMD in CKD patients. Further studies to elucidate the value of longitudinal assessments of ALP and BALP in CKD patients are warranted.

**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.

**Methods** We conducted a post hoc analysis using data from a phase 4 study of patients with end-stage renal disease (ESRD) and hyperphosphataemia 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/d; 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 g 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 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 1.5 g in approximately 75% of patients, which may have implications regarding vascular calcification.

**MP228 PARATHYROIDECTOMY IMPROVES RESTLESS LEG SYNDROME IN PATIENTS UNDER HEMODIALYSIS**

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**Introduction and Aims** Restless legs syndrome (RLS) is common among in-center hemodialysis patients and is associated with sleep disturbance and depression. The physiopathology of this syndrome is not completely understood and some authors have postulated that parathyroid hormone (PTH) and hyperphosphataemia may be implicated. Up to 80% of patients with RLS may present periodic leg movements of sleep (PLM), a well-known marker of mortality in patients under hemodialysis.

**Methods** This was a prospective cohort to evaluate the benefits of parathyroidectomy (PTx) on prevalence and severity of RLS, according to the International Restless Legs Syndrome Study Group (IRLSSG) rating scale (Brazilian Portuguese version). Overnight polysomnography was performed pre- and post-PTx (within 4 and 12 weeks, before and after surgery, respectively) in each patient, to access PLM. PLM was scored according to standard criteria (in summary: 4 or more leg movements with intervals greater than 5.0 and less than 90 seconds).

**Results** Eleven patients on hemodialysis with refractory hyperparathyroidism (PTH > 500 pg/ml, despite optimized clinical interventions) underwent PTx. Mean age was 49.6 ± 17.6 years, 36% were male. Pre- and post-PTx biochemical variables are
Hypovitaminosis D is highly prevalent among patients with nondialyzed 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 (eGFR) 30.8 ± 14.1 mL/minute, 35.2% 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 (>30 ng/ml) and hypovitaminosis D (<30 ng/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 and 14.1% had deficiency (<15 ng/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: 1.75; 95% CI: 1.04 to 2.96; 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 (ClaSS). First finding is all ClaSS have specific 'hourglass' shapes (figured). 'Hourglass' is enclosing red area for sample A and B 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.

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) (R² = 0.96) (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).

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% confidence intervals were all below 0.5, namely: PTH and all-cause mortality, 14 trials, -0.39 [-0.78, 0.20]; PTH and cardiovascular mortality, 6 trials, -0.04 [-0.73, 0.70]; calcium and all-cause mortality, 18 trials, 0.07 [-0.44, 0.55]; calcium and cardiovascular mortality, 9 trials, 0.17 [-0.52, 0.74]; phosphorus and all-cause mortality, 17 trials, -0.44 [0.75, 0.44] and phosphorus and cardiovascular mortality, 9 trials, -0.33 [-0.79, 0.36].

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.

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. 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 practicing 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.