Metabolic Bone Disease in the Elderly

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MBD + CKD in Elderly patients

- Our focus for today:
  - CKD-MBD (previously named Renal Osteodystrophy)
    - Low bone turnover (Adynamic Bone disease/ Osteomalacia)
    - High bone turnover (Osteitis Fibrosa)
  - Osteoporosis and CKD
Objectives

- Understand CKD-MBD and Osteoporosis in Elderly patients as a complex multi-system disorder
- Differentiate between and diagnose Osteoporosis and CKD-MBD
- Correlation between Osteoporosis and CKD
- Treatment approach to different stages of CKD-MBD
- Treatment of Osteoporosis in different CKD stages
Impact on Quality of life in patients with CKD-MBD and Osteoporosis

- Increased risk of fractures → Decrease quality of life → Increase mortality

- 2-3 fold increase in association of hip fracture with moderate to severe kidney dysfunction

- Hip fractures among elderly ESRD patients is four fold higher than general population.

- Mortality risk in Elderly ESRD patients with hip fracture is twice higher than patients without hip fracture

- Alem et Al, kidney Int 58: 396-399, 2000
Bone Cells

Osteoclast

Osteoblast

Osteocyte

Mesenchyme

Bone matrix

Newly formed matrix (osteoid)

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CKD-MBD: A Complex Multisystem Disorder

Laboratory abnormalities
- Elevated
  - FGF-23
  - PTH
  - Phosphorus
- Decreased
  - 1,25(OH)_2D_3
  - Calcium

CKD-MBD

Vascular and soft tissue calcification

Calcification

Bone disease

Abnormal bone
- Turnover
- Mineralization
- Volume
- Linear growth
- Strength

CKD-MBD = chronic kidney disease-mineral bone disorder; PTH = parathyroid hormone.
Vascular Calcification

- Uncontrolled CKD-MBD
- ESRD on HD for a long duration
- In HD patients associated with increased mortality by 17%
- Prevention and early treatment in Geriatric population is a key
Pathophysiology of MBD

CKD-MBD High vs Low bone turnovers
Osteoporosis in elderly
Osteomalacia
Normal Calcium and phosphorus regulation

Normal kidney function: schematic representation of the interaction of the different PTH-regulating factors.

John Cunningham et al. CJASN 2011;8:913-921
CKD and SHPT

Renal failure: schematic representation of the interaction of the different PTH regulating factors.

John Cunningham et al. CJASN 2011;6:913-921

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High Turnover bone disease

Pathophysiology of Secondary Hyperparathyroidism

Bone disease and systemic toxicity

Both FGF-23 and PTH are phosphaturic

Calcium

1,25(OH)₂D₃

Phosphorus

Chronic Kidney Disease

Progression of iPTH, Corrected Ca, and P Levels Study for the Evaluation of Early Kidney Disease (SEEK)

Prospective, observational, multi-center study

N = 1814
Progression of iPTH, Corrected Ca, and P Levels Study for the Evaluation of Early Kidney Disease (SEEK)

Persistent SHPT leads to Parathyroid hyperplasia

Development of parathyroid hyperplasia.

John Cunningham et al. CJASN 2011;6:913-921
Low Bone Turnover

Pathogenesis of Adynamic Bone Disease

Better phosphate control
Diabetes
↑ Age
↑ Aluminum
Vitamin D therapy
VDR polymorphism
CAPD

Relative hypoparathyroidism
Decreased bone formation rate

↑ Serum Ca
↑ Calcium intake

Diabetes
↑ Age
Uremic toxins
Altered growth factors and cytokines
Malnutrition
↑ Aluminum
Vitamin D therapy
↓ PTH-1 receptor

Modified from reference 68.
Osteoporosis pathophysiology


- Genetic factors
- Physical activity
- Nutrition

Peak Bone Mass

Menopause
- Decreased serum estrogen
- Increased IL-1, IL-6, TNF levels
- Increased expression of RANK, RANKL
- Increased osteoclast activity

Aging
- Decreased replicative activity of osteoprogenitor cells
- Decreased synthetic activity of osteoblasts
- Decreased biologic activity of matrix-bound growth factors
- Reduced physical activity

Osteoporosis
SKELETAL ABNORMALITIES RELATED TO CKD-MBD and Osteoporosis
High Turnover

- **Osteitis Fibrosa:**
- **SHPT**
- Increased osteoclast and osteoblast activity.
- peritrabecular fibrosis.
- Normal mineralization.
- MCC in AA
Low-Turnover Bone disease

- More likely in Geriatric and diabetic population
- More than 40% in CKD stage 5 are affected.
- High association with cardiovascular calcification and mortality
- Fracture incidence is estimated to be TWICE higher compared to high-bone turnover disorders
- More common in PD patients due to high dialysate calcium exposure
Low Turnover- Adynamic Bone disease

- Low bone turnover
- Acellularity
- MCC in Elderly Caucasians
Low Turnover- Osteomalacia

- defective mineralization of newly formed osteoid
- Vitamin D def. and Aluminum deposition
- Very common in Geriatric patient
Mixed Renal Osteodystrophy

- It encompasses increased bone turnover with abnormal mineralization
Osteoporosis

- Low bone mineral mass and skeletal fragility
- May have low, normal or even high bone turnover
- Loss of bone structure
- MCC in elderly caucasian women
Clinical manifestations and evaluation of CKD-MBD and osteoporosis in Elderly
Clinical manifestations in Renal Osteodystrophy

- Aches and pains are most common.
- Arthritis.
- Fractures (wrist, spine and hip)
- Kyphoscoliosis or chest wall deformities.
- Pruritus due to hyperparathyroidism
- Calciphylaxis
Biochemical markers in CKD-MBD

- Serum Ca or ionized Ca$^{++}$
- Phosphorus level
- Ca X Phos (vascular and tissue calcification)
- iPTH assay
- 25-hydroxyvitamin D$_3$ levels
- 1,25-dihydroxyvitamin D$_3$ levels (check once)
- Alkaline phosphatase (marker for osteoblast activity)
- Bone specific alkaline phosphatase (BSAP)
- Bicarbonate (metabolic acidosis)
CKD-MBD biomarkers

High Turnover

- High Phos/High FGF-23
- High phosphaturia
- Low Calcium
- High PTH
- High Alk phos/BSAP
- Low Calcitriol levels

Low Turnover

- Normal or slightly high phos and calcium
- Low PTH <100 pg/ml
- Low or downward trends in Alk Phos/BSAP
- High 25-hydroxyvitamin D₃ levels (on ergocalciferol)
- High Hemoglobin A₁c
Non invasive Imaging

- Routine X-ray is insensitive for ROD.
- DEXA is used to
  - assess mineral bone density in osteoporosis
  - Not used in ROD
  - Unable to differentiate between cortical and trabecular
- Heel Ultrasound
  - Used in osteoporosis
- Quantitative CT scan
  - Able to distinguish the outer dense cortical bone from inner spongy trabecular bone.
Is eGFR included in FRAX?
Transiliac Bone biopsy

- Unexplained fractures, persistent bone pain, unexplained hypercalcemia, high PTH but low Alk Phos
- Advantages:
  - Gold standard
  - Differentiates between ADB and Osteoporosis.
  - Allow physicians to formulate a future treatment plan
- Disadvantages:
  - Invasive in the elderly
  - Needs a great deal of expertise
Treatment of CKD-MBD
Treatment of High-turnover Bone Disease

- Prevention of secondary hyperparathyroidism is the primary goal! Initiate in stage 3 CKD.
- Prevention of hypocalcemia in CKD
  - Calcium carbonate
  - Calcitriol
- Control of phosphate
  - Dietary phosphate restriction in stage 2 or 3. Do not restrict meat and protein could lead to malnutrition.
  - Use of phosphate binders
Phosphate Binders..

- Calcium-containing antacids:
  - carbonate or acetate → Nephrolithiasis in elderly + milk-alkali syndrome
  - Limit dose 1500mg/day. **Inexpensive!!**
  - Association with increase risk of Vascular calcification
- Non-calcium-containing phosphate binders
  - Sevelamer carbonate or Hydrochloride → Fecal impaction and ileus.
  - Lanthanum
  - **Expensive** but decrease progression of vascular calcification.
Vitamin D 25 OH

- Very common def. in Geriatric population with CKD/ESRD
- Synthesis/inadequate intake/malnutrition/Inactive lifestyle
- Deficiency has been linked to CV events in PD and MI in elderly men.
- Supplementation has reduced hip fracture, but increase kidney stones in elderly
- CKD 3 to 5: recommend Vitamin D levels >30 ng/ml.
- No CKD: recommend vitamin D intake 800-1000 IU/D.

Active Vitamin D Metabolites: Calcitriol & Paricalcitol (Zemplar)

- lowers PTH levels, but increases Ca x phos
- Improves bone histology in CKD stage 3-4.
- It might not be effective in parathyroid hyperplasia
- Shoben et al demonstrated oral calcitriol use in non dialysis patients was associated with 26% lower risk for death.
- Avoid over correction strategy → Hypercalcemia!!

Role of Calcimimetics (Cinacalcet)

- How does it work?
- Works within minutes
- Decreases Ca x phos
- Recommended if iPTH > 300pg/ml,
- Side effects: nausea/vomiting (administered at night)
- Reduces rates of parathyroidectomies and calciphylaxis by 50%
Does Cinacalcet improve vascular calcification?

The ADVANCE study: a randomized study to evaluate the effects of cinacalcet plus low-dose vitamin D on vascular calcification in patients on hemodialysis

Paolo Raggi¹, Glenn M. Chertow², Pablo Urena Torres³, Botond Csiky⁴, Agostino Naso⁵, Kaldun Nossuli⁶, Moustafa Moustafa⁷, William G. Goodman⁸, Nicole Lopez⁸, Gerry Downey⁹, Bastian Dehmel¹⁰, Jürgen Floege¹¹ and on behalf of the ADVANCE Study Group

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Correspondence and offprint requests to: Paolo Raggi; E-mail: praggi@emory.edu
Design

- Prospective, randomized, controlled study
- Purpose: compare the progression of vascular and cardiac valve calcification in 360 HD patients with sHPT
- All patients were matched by baseline labs
- Subjects with CAC and aorta and cardiac valve calcium scores were determined both by Agatston and volume scoring using MDCT
- Subjects with Agatston CAC > 30 were randomized to receive Cinacalcet (30→180 mg/d) plus low dose calcitriol < 2ug.
- Primary end point was percentage change in Agatston CAC score from baseline to week 52
Study design.

Cinacalcet plus low-dose vitamin D group n=180

Flexible vitamin D group n=180

Day 1 W4 W8 W12 W16 W20 W28 MDCT scan W52 MDCT scan

180 mg

120 mg

90 mg

60 mg

30 mg

Results

- Median Agatston CAC scores increased 24% in the C+D group and 31% in D group $P=0.073$ and changes in Volume CAC scores were 22% in C + D group vs 30% in D group with $P=0.009$

- Increases in calcification scores were consistently less in the aorta, aortic valve, and mitral valve among subjects treated with Cinacalcet + Vit D group compared to vit D group.

- Conclusion: In HD patients with moderate to severe sHPT, cinacalcet + low dose of Vit D may attenuate vascular and cardiac valve calcification.
The median percent change (IQR) from baseline values in Agatston calcification scores over 52 weeks in each treatment group: (A) total coronary artery, (B) thoracic aorta, (C) aortic valve and (D) mitral valve.


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Role of Parathyroidectomy in Elderly
“Subtotal removal”

- Assess for functional status, risks and benefits
- High risk for Hungry bone syndrome
- Indications for Parathyroidectomy
  - Severe Hyperparathyroidism
    - With persistent hyperphosphatemia
    - Unresponsive to Calcitriol and calcium
    - Persistent hypercalcemia (Tertiary hyperparathyroidism)
    - Intolerance to Calcimimetics
  - Renal transplant candidate
    - Evidence of metastatic calcification
  - Calciphylaxis with evidence of hyperparathyroidism
  - Severe pruritus
Overall therapy strategy plan

Comprehensive clinical nephrology by Richard J Johnson 5th edition

Treatment of Renal Osteodystrophy at Various Stages of Renal Impairment

- Monitor Ca/P/iPTH levels
- Evaluate vitamin D status and treat as necessary
- Treat acidosis

Consider:
- Dietary Pi restriction
- P binders

CKD 3

Consider:
- Active vitamin D sterols
- Limiting Ca intake

CKD 4

Consider:
- Parathyroidectomy
- Calcimimetic*
- Dialysis regimen*
- Dialysate calcium*

CKD 5

Modified from reference 67.
Treatment of Adynamic Bone Disease

- Goals:
  - Restore adequate PTH levels
  - Reduce active vitamin D (always check PTH levels)
  - Avoid calcium-containing phosphate binders & dialysate calcium concentration to 1.25mmol/L

- Consider change from PD to HD
- Aggressive Diabetes management
- Recombinant PTH (Teriparatide) ➔ orthostatic hypotension
- Future direction: Calcilytics (i.e. – calcium receptors antagonists ➔ increased PTH secretion ➔ anabolic effect on bone tissue, increasing volume and bone density
The Effects of Cinacalcet in Older and Younger Patients on Hemodialysis: The Evaluation of Cinacalcet HCl Therapy to Lower Cardiovascular Events (EVOLVE) Trial

Design

• Evaluation of Cinacalcet HCT to lower Cardiovascular events (EVOLVE) was a global, multicenter, randomized placebo-controlled trial in 3883 prevalent patients on hemodialysis

• Examined the effects of cinacalcet in older patients >65 years n=1005 and younger patients <65 n=2878

• Primary endpoint was death, major CV events, and development of severe HPT
Results

- Older patients had higher baseline prevalence of DM and CV co-morbidity
- Higher rates of Kidney transplant and parathyroidectomy were > 3 fold higher in younger relative to older patients and more frequent than placebo
- Adjusted relative hazard for Primary composite CV end point was 0.70 for older patients compared to 0.97 in younger patients
- Adjusted relative hazard for mortality was 0.68 in older vs 0.99 in younger
- Reduction risk of severe unremitting HPT was similar in both group
Osteoporosis in CKD Elderly
Osteoporosis in CKD

- Osteoporosis may co-exist with CKD-MBD

- Important to differentiate between osteoporosis & CKD-MBD

Note: both are associated with increased mortality
Osteoporosis in Elderly with CKD

- Difficult to diagnose osteoporosis in the setting of CKD.
- DEXA measures bone mineral density only.
- True or False: DEXA predicts the histomorphology of the bone in CKD patients or CKD-MBD?
Diagnosis of Osteoporosis in CKD

Based on experts opinion and KDIGO (Kidney Disease improving global outcomes)

True or False: DEXA predicts the histomorphology of the bone in CKD patients or CKD-MBD?

- KDIGO
- Miller et al, Seminars in Nephrology vol 29, no. 2, pp.144-155, 2009
Diagnosis of Osteoporosis in Elderly patient with CKD

- **Start with Biochemical markers**
  - Check BSAP/ Ca/phosp/PTH/Alk Phos
    - BSAP Level < 7 ng/ml and PTH < 100um/ml is concerning for ADB
- **Elderly patients with GFR > 30**
  - If no Biochemical markers abnormalities
  - Use DEXA T-score or fragility fracture

- KDIGO
- Miller et al, Seminars in Nephrology vol 29, no. 2, pp.144-155, 2009
Diagnosis of Osteoporosis in Elderly patient with CKD

- **Elderly patients with GFR< 30 and dialysis**
  - check for biochemical abnormalities.
  - DEXA is not recommended due to calcified soft tissue giving confounding results
  - Recommend bone biopsy
  - studies ongoing regarding quantitative radial CT scan

- KDIGO
- Miller et al, Seminars in Nephrology vol 29, no. 2, pp.144-155, 2009
Treatment of Osteoporosis in CKD

- **Lifestyle evaluation to prevent falls**

- **Calcium & vitamin D**
  - Patients with CKD eGFR> 30:
    - Ca should not exceed 2000 mg/day
  - Patients with CKD eGFR< 30: avoid hypercalcemia and high calcium load
  - Ca = 1200 mg/day
  - Cholecalciferol or Ergocalciferol: 800 IU per day

- **Hormone replacement therapy??**
Treatment of Osteoporosis in CKD

- **Bisphosphonates (renally cleared)**
  - Use is controversial
  - Nephrotic syndrome
  - AKI due to bisphosphonate induced ATN

- **Denosumab (NOT renally cleared)**
  - Severe Hypocalcemia
• **Patients with GFR > 30**
  • Does the patient has CKD-MBD? If
    • Yes, treat CKD-MBD first
    • No, treat with bisphosphonate

• **Patients with GFR < 30**
  • Does the patient has CKD-MBD?
    • Yes: treat CKD-MBD first
    • No, treat with a short- duration bisphosphonates or Denosumab
  • Limit treatment to 3 years
Are Bisphosphononates safe in CKD?

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Safety and Efficacy of Risedronate in Patients With Age-Related Reduced Renal Function as Estimated by the Cockcroft and Gault Method: A Pooled Analysis of Nine Clinical Trials

Paul D Miller,¹ Christian Roux,² Steven Boonen,³ Ian P Barton,⁴ Lisa E Dunlap,⁴ and David E Burgio⁴

ABSTRACT: The incidences of osteoporosis and renal insufficiency increase with age. We studied the influence of renal function on the safety and efficacy of risedronate 5 mg daily in osteoporotic women. Risedronate was safe and effective in osteoporotic women with mild, moderate, or severe age-related renal impairment.
Design

- Retrospective analysis, mean age was 75 years.
- Combined data from nine randomized, double-blind, placebo-controlled phase III risedronate trials were analyzed.
- Renal impairment was estimated by Cockcroft-Gault method
  - GFR 80-50 ml/min → mild (48%)
  - GFR 50-30 ml/min → moderate (45%)
  - GFR < 30 ml/min → severe (7%)
- 4500 participants received placebo x 3 yrs
- 4496 participants received Risedronate 5 mg p.o daily x 3yrs
- All patients were on vitamin D 500 IU, calcium 1 gram
- DEXA scan done at baseline, 6, 12, and 24 months
### Incidence of Adverse Events in Patients With Renal Impairment Who Were Treated With Placebo or Risedronate 5 mg Daily

<table>
<thead>
<tr>
<th>Renal impairment subgroup</th>
<th>Placebo</th>
<th>Risedronate 5 mg</th>
<th>Relative risk (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe (&lt;30 ml/min)†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>271</td>
<td>301</td>
<td></td>
</tr>
<tr>
<td>All adverse events, n (%)</td>
<td>246 (91%)</td>
<td>262 (87%)</td>
<td>0.96 (0.91, 1.02)</td>
</tr>
<tr>
<td>Urinary- and renal function–related adverse events, n (%)§</td>
<td>55 (20%)</td>
<td>57 (19%)</td>
<td>0.93 (0.67, 1.30)</td>
</tr>
<tr>
<td>Specific renal function–related adverse events, n (%)§</td>
<td>9 (3%)</td>
<td>8 (3%)</td>
<td>0.80 (0.31, 2.04)</td>
</tr>
<tr>
<td>Moderate (≥30 to &lt;50 ml/min)†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>2037</td>
<td>2034</td>
<td></td>
</tr>
<tr>
<td>All adverse events, n (%)</td>
<td>1834 (90%)</td>
<td>1859 (91%)</td>
<td>1.02 (0.99, 1.04)</td>
</tr>
<tr>
<td>Urinary- and renal function–related adverse events, n (%)§</td>
<td>363 (18%)</td>
<td>363 (18%)</td>
<td>1.00 (0.88, 1.14)</td>
</tr>
<tr>
<td>Specific renal function–related adverse events, n (%)§</td>
<td>32 (2%)</td>
<td>28 (1%)</td>
<td>0.88 (0.53, 1.45)</td>
</tr>
<tr>
<td>Mild (≥50 to &lt;80 ml/min)†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>2192</td>
<td>2161</td>
<td></td>
</tr>
<tr>
<td>All adverse events, n (%)</td>
<td>2012 (92%)</td>
<td>1997 (92%)</td>
<td>1.01 (0.99, 1.02)</td>
</tr>
<tr>
<td>Specific renal function–related adverse events, n (%)§</td>
<td>34 (2%)</td>
<td>21 (1%)</td>
<td>0.63 (0.37, 1.07)</td>
</tr>
<tr>
<td>Urinary- and renal function–related adverse events, n (%)§</td>
<td>396 (18%)</td>
<td>376 (17%)</td>
<td>0.96 (0.85, 1.09)</td>
</tr>
</tbody>
</table>

N = total number of patients in renal impairment subgroup; n = number of patients with adverse events.

* Risk in risedronate group relative to placebo group.
† Creatinine clearance estimated using the Cockcroft and Gault method.²³
§ Specific renal function–related adverse events included hematuria, hydronephrosis, kidney failure, acute kidney failure, abnormal kidney function, uremia, oliguria, polyuria, glomerulitis, and nephritis.
⁸ Urinary- and renal function–related adverse events included specific renal function–related adverse events plus other events from the COSTART urogenital body system that were related to urinary function or kidney disease.²⁵
Results

- No significant change in serum Ca, phos, creatinine from the baseline to endpoint
- No significant adverse events compared between placebo and CKD
- In all 3 subgroups, risedronate effectively preserved BMD and reduced the incident of vertebral fractures.

*Journal of Bone and Mineral Research*  
*Volume 20, Issue 12, pages 2105-2115, 22 AUG 2005 DOI: 10.1359/JBMR.050817  
Baseline Characteristics for Patients With Renal Impairment Treated With Placebo or Risedronate 5 mg Daily

<table>
<thead>
<tr>
<th></th>
<th>Severe (&lt;30 ml/min)</th>
<th>Moderate (&gt;30 to &lt;50 ml/min)</th>
<th>Mild (&gt;50 to &lt;80 ml/min)</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Risedronate</td>
<td>Placebo</td>
<td>Risedronate</td>
</tr>
<tr>
<td>N</td>
<td>271</td>
<td>301</td>
<td>2037</td>
<td>2034</td>
</tr>
<tr>
<td>Age (years)</td>
<td>83 (5.5)</td>
<td>83 (5.8)</td>
<td>78 (6.1)</td>
<td>77 (6.2)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>152 (7.0)</td>
<td>151 (7.7)</td>
<td>155 (6.7)</td>
<td>155 (6.8)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>51 (8.9)</td>
<td>51 (8.9)</td>
<td>58 (9.1)</td>
<td>58 (9.4)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>22 (3.7)</td>
<td>22 (3.8)</td>
<td>24 (3.8)</td>
<td>24 (3.9)</td>
</tr>
<tr>
<td>Femoral neck T score</td>
<td>-3.10 (0.608)</td>
<td>-3.15 (0.716)</td>
<td>-2.74 (0.657)</td>
<td>-2.74 (0.662)</td>
</tr>
<tr>
<td>Lumbar spine T score</td>
<td>-2.93 (1.136)</td>
<td>-3.23 (1.566)</td>
<td>-2.75 (1.286)</td>
<td>-2.78 (1.220)</td>
</tr>
<tr>
<td>≥1 prevalent vertebral fractures</td>
<td>64%</td>
<td>57%</td>
<td>54%</td>
<td>58%</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1.30 (0.241)</td>
<td>1.34 (0.293)</td>
<td>1.04 (0.173)</td>
<td>1.05 (0.179)</td>
</tr>
<tr>
<td>Range</td>
<td>0.70-2.14</td>
<td>0.78-2.67</td>
<td>0.60-1.74</td>
<td>0.60-1.90</td>
</tr>
<tr>
<td>Creatinine clearance (ml/min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>27.2</td>
<td>26.4</td>
<td>41.4</td>
<td>41.5</td>
</tr>
<tr>
<td>Range</td>
<td>14.1-29.8</td>
<td>13.2-29.9</td>
<td>30.0-49.9</td>
<td>30.0-49.9</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>24.5-28.7</td>
<td>23.1-28.5</td>
<td>36.8-45.7</td>
<td>36.7-45.8</td>
</tr>
<tr>
<td>Duration of treatment (months)</td>
<td>22 (13.8)</td>
<td>25 (13.5)</td>
<td>25 (13.5)</td>
<td>25 (12.7)</td>
</tr>
</tbody>
</table>

* Creatinine clearance estimated using the Cockcroft and Gault method (23)
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http://onlinelibrary.wiley.com/doi/10.1359/JBMR.050817/full#fig1
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http://onlinelibrary.wiley.com/doi/10.1359/JBMR.050817/full#fig2
Bisphosphonates in HD

- Severe adverse events
- Hypocalcemia
- Osteonecrosis of the jaw
- Can be still found in bones for up to 8 years
- Not recommended for Elderly patients on HD.
Denosumab - Prolia

- Monoclonal antibody binds to receptor activator of nuclear factor Kappa-B ligand, inhabiting osteoclast formation
- No need to renally dose
- Associated with life threatening hypocalcemia and seizures in elderly.

McCormick et al, Am J Kidney disease 2012;60:626-8
Summary

- CKD-MBD is a multisystem disorder including renal osteodystrophy AND vascular calcification
- Presence of CKD-MBD is an independent predictor of mortality in the elderly
- Early recognition risks for CKD-MBD is key to prevention
- Differentiating low-bone turnover from high-bone turnover disease determines course of treatment
- Osteoporosis and CKD-MBD may co-exist and it’s vital to differentiate the two
- Treatment of Osteoporosis depends on the CKD stage, risks and benefits
Thank you.