Diagnosis and management of Osteoporosis in CKD

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Diagnosis and Management of Osteoporosis in CKD

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Bone Cast Feb, 20212

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Disclosures

• Pieter Evenepoel declares that he served as a consultant for or received honoraria and research support from:
  – Amgen
  – VifoFMC
  – Medice

• Kassim Javaid declares that he served as a consultant for or received honoraria and research support from:
  • Amgen
  • UCB
  • Kyowa Kirin

Views are of the authors
Case studies  1a Thomas

- Fragility fracture with known renal impairment
  - 68 year old with 2020 Humeral fracture
  - 2016 Elbow fracture
  - 2016 DXA LS -1.3 FN -0.1 TH -0.3

- Ht 175 cm
- Wt 139.5 kg
- Diabetes Ty2
- Nephrotic range proteinuria
- Ex-smoker with COPD, high alcohol intake
- Peripheral vascular disease
Case studies 1a Thomas

- Fragility fracture with known progressive renal impairment
Case studies 1b Mary

- Fragility fracture with previously undiagnosed renal impairment

- 86 year old with 2020 humeral fracture
- 2015 metatarsal fracture

- Ht 163 cm
- Wt 54 kg
- Mild cognitive impairment

- eGFR 21
- CrCl 14
Case studies 2- Joseph

- Already on Anti-osteoporosis therapy developing renal impairment
- 90 year old male
- 2015 ankle fracture 2016 wrist fracture > eGFR only 30
  - Not for bishosphonatess > start denosumab > now 5 years later has CKD 4/5
Diagnosis and Management of Osteoporosis in CKD

• CKD-MBD
• Assessment of bone health in advanced CKD
• Therapeutic approach in patients with advanced CKD presenting with bone fragility/osteoporosis
• Conclusions- take home messages

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.71 (1.28-2.18)</td>
<td>1.78 (1.35-2.25)</td>
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<tr>
<td>2</td>
<td>2.70 (2.17-3.24)</td>
<td>3.24 (2.61-3.88)</td>
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<tr>
<td>3</td>
<td>5.42 (4.89-5.95)</td>
<td>7.69 (7.02-8.36)</td>
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<tr>
<td>4</td>
<td>0.21 (0.15-0.27)</td>
<td>0.35 (0.25-0.45)</td>
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<tr>
<td>5</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td>10.03 (9.16-10.91)</td>
<td>13.07 (12.04-14.10)</td>
</tr>
</tbody>
</table>

Hypertension: 33.3%
Diabetes: 10.6%
Clinical CVD: 36.3%

Advanced CKD = CKD G4-5D (eGFR<30 ml/min 1.73m²)

CKD-MBD

Moe SM et al. Kidney Int 2006
Pathophysiology of ROD

Renal disease

FGF23↑

CYP24A1

FA

phos↓

PTH

↑

FA

Ca↓

1,25(OH)2D↓

Ca↓

FEphos↑

CYP24A1

CYP27B

P

PTH resistance

Inflammation/oxidative stress

Gut dysbiosis

Hypogonadism

Metabolic acidosis

PTH resistance

ROD

1,25(OH)2D

Ca

FAphos↓

FA

Ca↓


Courtesy P Evenepoel


P

PTH

Calcitriol

FGF23

P

Ca

# Epidemiology of ROD (according to TMV classification)

<table>
<thead>
<tr>
<th></th>
<th>Portugal¹</th>
<th>Sao Paolo²</th>
<th>KDIGO consortium³</th>
<th>Consortium⁴</th>
<th>Leuven-Antwerp⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>68</td>
<td>97</td>
<td>492</td>
<td>630</td>
<td>36</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54.5</td>
<td>49.5 ± 13.1</td>
<td>49.5 ± 15.1</td>
<td>55.0 ± 1.0</td>
<td>55.5 ± 12.3</td>
</tr>
<tr>
<td>White race (%)</td>
<td>97</td>
<td>58</td>
<td>94</td>
<td>86</td>
<td>100</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>59</td>
<td>65</td>
<td>57</td>
<td>52</td>
<td>73</td>
</tr>
<tr>
<td>Dialysis vintage (years)</td>
<td>2</td>
<td>3.1 ± 2.3</td>
<td>4.7 ± 3.7</td>
<td>4.3 ± 0.2</td>
<td>2.2 (1.2–2.9)</td>
</tr>
<tr>
<td>Ca (mg/dL)</td>
<td>9.7</td>
<td>9.5 ± 1.0</td>
<td>9.2</td>
<td>9.2</td>
<td>9.2 ± 0.8</td>
</tr>
<tr>
<td>Phos (mg/dL)</td>
<td>5.8</td>
<td>5.4 ± 1.5</td>
<td>5.8 ± 1.9</td>
<td>5.3</td>
<td>4.44 ± 1.13</td>
</tr>
<tr>
<td>PTH × UNL</td>
<td>2.0</td>
<td>5.3</td>
<td>8.3</td>
<td>4.2</td>
<td>4.8</td>
</tr>
</tbody>
</table>

**Turnover**

- Low: 0%
- Normal: 63%
- High: 37%

- Low: 3%
- Normal: 60%
- High: 37%

- Low: 4%
- Normal: 20%
- High: 17%

- Low: 59%
- Normal: 24%
- High: 17%

- Low: 53%
- Normal: 44%
- High: 3%

Epidemiology of fractures in CKD


Bone health and fracture risk in CKD

• Fracture burden in advanced CKD
• Assessment of bone health in advanced CKD
• Therapeutic approach in patients with advanced CKD presenting with bone fragility/osteoporosis
• Conclusions- take home messages
Assessment of bone health and fracture risk in CKD

General assessment
- Kidney function (KDIGO grading)
- Mineral metabolism (Ca-phos-PTH-25(OH)D, ALP)
- Nutritional status (Ca-intake)
- Acid-base status (Gonadal status)

Bone biomarkers
- DEXA
- XR (VFA)
- TBS
- (hr-)pQCT

Clinical risk scores

Bone biopsy
- Double labelled?
- Looking for Adynamic
- High resorption
- Osteomalacia
Some doubts remain as to the consistency of the fracture risk prediction by DXA across stages of CKD and degree of PTH control.


DXA: validity?
Inappropriate high PTH mainly affects cortical bone.

Reliability

T score for distal radius
Sources of Bias

- Aortic calcification
- Scoliosis
- Hypertrophic degenerative disease
- Compression fractures
- Calcium, barium, or lanthanum within the gastrointestinal tract
- Renal lithiasis
- Focal sclerotic bone lesions

• AV fistula

Table 3. BMD and T- or Z-scores at both forearms

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Radius</th>
<th>AVF/Non-AVF Forearm</th>
<th>All Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Value</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>33%</td>
<td>AVF</td>
<td>0.425 ± 0.080</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Non-AVF</td>
<td>0.454 ± 0.087</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean difference</td>
<td>0.029⁣</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AVF</td>
<td>0.429 ± 0.076</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal</td>
<td>0.456 ± 0.083</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean difference</td>
<td>0.027⁣</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AVF</td>
<td>0.234 ± 0.082</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal</td>
<td>0.257 ± 0.090</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean difference</td>
<td>0.023</td>
</tr>
<tr>
<td>T- or Z-score</td>
<td>33%</td>
<td>AVF</td>
<td>-2.5 ± 1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal</td>
<td>-2.1 ± 1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean difference</td>
<td>0.7 ± 1.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AVF</td>
<td>1.2 ± 2.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal</td>
<td>1.2 ± 2.0</td>
</tr>
</tbody>
</table>

LSC calculated in control group.
*Mean difference > LSC; therefore, a statistically significant change.

Does DXA inform on ROD subtype?

BMD:
- Normal Bone Volume: 1.250 g/cm²
- Low Bone Volume: 0.750 g/cm²

Type of bone:
- Normal
- Osteoporosis
- Osteomalacia
- HPT

Adapted from Urena-Torres P et al. Semin Nephrol 34:612-625, 2014
The International Society for Clinical Densitometry (ISCD) guidelines recommend lateral Spine imaging with Standard Radiography or Densitometric vertebral fracture assessment (VFA) when T-score is $<-1.0$ and if one or more of the following is present:

- Women age $\geq 70$ years or men $\geq$ age 80 years
- Historical height loss $> 4$ cm ($>1.5$ inches)
- Self-reported but undocumented prior vertebral fracture
- Glucocorticoid therapy equivalent to $\geq 5$ mg of prednisone or equivalent per day for $\geq 3$ months
Long-Term Atherosclerotic Vascular Disease Risk and Prognosis in Elderly Women With Abdominal Aortic Calcification on Lateral Spine Images Captured During Bone Density Testing: A Prospective Study

Joshua R Lewis,1,2,4,8 John T Schousboe,2,5,6 Wai H Lim,3,6,7 Germaine Wong,2,7 Kevin E Wilson,1 Kun Zhu,1,8 Peter L Thompson,9 Douglas P Kiel,10 and Richard L Prince11,12

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3Medical School, University of Western Australia, Sir Charles Gairdner Hospital UWA, Perth, Australia
4Park Nicollet Clinic and HealthPartners Institute, HealthPartners, Minneapolis, MN, USA
5Division of Health Policy and Management, University of Minnesota, Minneapolis, MN, USA
6Department of Renal Medicine, Sir Charles Gairdner Hospital, Perth, Australia
7Skeletal Health, Hologic, Inc., Marlborough, MA, USA
8Department of Endocrinology and Diabetes, Sir Charles Gairdner Hospital, Perth, Australia
9Department of Cardiology, Sir Charles Gairdner Hospital, Perth, Australia
10Institute for Aging Research, Hebrew SeniorLife, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

ABSTRACT
Lateral spine images are captured using bone densitometers for vertebral fracture assessment (VFA) in older women. Abdominal aortic calcification (AAC) is commonly seen on these images; however, the long-term prognosis in women with AAC remains uncertain. In a prospective study of 1052 community-dwelling ambulant white women over 70 years old abdominal aortic calcification (AAC) scores were calculated from digital lateral spine images captured during bone density testing in 1998 or 1999. Cardiovascular risk factors were assessed in 1998, whereas 14.5-year atherosclerotic vascular disease (ASVD)-related hospitalisations and deaths (events) were available through linked health records. Using established cut points for AAC: (1) women with high AAC had low AAC (AAC24 score 0–1), 387 (38%) moderate AAC (AAC24 score 2–3), and 197 (19%) had high AAC (AAC24 score >3). Over 14.5 years, 420 women experienced an ASVD event. Increasing severity of AAC was associated with increased absolute risk of ASVD events (37%, 59%, and 49%, respectively, p < 0.008 for trend), ASVD deaths (15%, 21%, and 27%, respectively, p < 0.001 for trend), and all-cause mortality (30%, 38%, and 44%, respectively, p < 0.001 for trend). After adjusting for Framingham risk scores, women with high AAC had increased relative hazard for ASVD events (HR 1.37 95% CI, 1.07 to 1.77, p = 0.0013) compared to women with low AAC. Similarly, women with moderate AAC and high AAC had increased relative hazards for ASVD deaths (HR 1.41 95% CI, 1.03 to 1.94, p = 0.034) and HR 1.80 (95% CI, 1.26 to 2.57, p = 0.005), or any deaths HR 1.30 (95% CI, 1.03 to 1.64, p = 0.026) and HR 1.53 (95% CI, 1.17 to 2.02, p = 0.003), compared to women with low AAC. In conclusion, more advanced AAC on images captured for VFA is associated with long-term ASVD hospitalisations and deaths, before and after adjusting for Framingham risk scores. AAC assessment could be considered in addition to VFA to identify individuals who may benefit for more aggressive cardiovascular primary prevention strategies. © 2018 American Society for Bone and Mineral Research

KEY WORDS: AGING; CARDIOVASCULAR DISEASE; EPIDEMIOLOGY
Assessment of bone health and fracture risk in CKD

**General assessment**
- Kidney function (KDIGO grading)
- Mineral metabolism (Ca-phos-PTH-25(OH)D)
- Nutritional status (Ca-intake)
- Acid-base status (Gonadal status)

**Imaging**
- DEXA
- (hr-)pQCT
- XR (VFA)
- TBS

**Bone biomarkers**

**Bone biopsy**

**Clinical risk scores**
Further studies in different/unselected CKD cohorts are mandatory to define whether arithmetic adjustments of the FRAX score have to be made with knowledge of advanced CKD.
Assessment of bone health and fracture risk in CKD

General assessment
- Kidney function (KDIGO grading)
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Imaging
- DEXA
- (hr-)pQCT
- XR (VFA)
- TBS

Bone biomarkers

Bone biopsy

Clinical risk scores
Bone turnover markers

Clinical utility
- Prognostication
  - Fractures
  - Bone loss
- Treatment decision (T-category)
- Treatment response

Performance
- Moderate
  - Moderate/good
  - Good
- High NPV, rather poor PPV
- Good

PINP, Procollagen I N - Terminal Propeptide.

Assessment of bone health and fracture risk in CKD

General assessment
- Kidney function (KDIGO grading)
- Mineral metabolism (Ca-phos-PTH-25(OH)D)
- Nutritional status (Ca-intake)
- Acid-base status
- (Gonadal status)

Bone biomarkers

Imaging
- DEXA
- (hr-)
- pQCT
- XR (VFA)
- TBS

Clinical risk scores

Bone biopsy
Bone biopsy

General anesthesia/local anesthesia ± light sedation

BiopsyBell needle, 3.8 mm inner diameter (7G)
Horizontal (trans)iliac approach
Bone biopsy: SWOT analysis

**Strengths**
Gold standard to assess bone health (TMV-µarchitecture)

**Weaknesses**
Invasive-laborious
Link with bone outcomes missing

**Opportunities**
Small needles

**Threats**
Waning expertise
Bone health and fracture risk in CKD

• Fracture burden in advanced CKD
• Assessment of bone health in advanced CKD
• Therapeutic approach in patients with advanced CKD presenting with bone fragility/osteoporosis
• Conclusions- take home messages
As in the general population

Lack of evidence (from RCT)

Fear for complications

Lack of knowledge of the underlying pathophysiology

OSTEOPOROSIS

CKD1  CKD2  CKD3  CKD4  CKD5  CKD5D
Non-pharmacological therapy & lifestyle modification

Physical activity  Fall prevention
## Pharmacological therapy

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Renal retention</th>
<th>Efficacy Preclinical</th>
<th>Post hoc (postmenopausal women)</th>
<th>Clinical trial (advanced CKD)</th>
<th>Safety (postmenopausal women)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Romosozumab</td>
<td>Unlikely</td>
<td>Yes, low PTH only [162]</td>
<td>No data</td>
<td>No data</td>
<td>Cardiovascular adverse events ↑ [165] (hypocalcaemia)</td>
<td>Beware: offset of effect</td>
</tr>
</tbody>
</table>
Antiresorptives: key messages

- Binding to Hydroxy-apatite
  - Non nitrogen (clodronate / etidronate)
  - Nitrogen (alendronate, risedronate, ibandronate, zoledronate)
Distribution

- Bisphosphonate
- Unmetabolized

Passive glomerular filtration
Proximal tubular active secretion

Local skeletal release and re-attachment
Preferential uptake into resorbing bone with more exposed hydroxyapatite.

Renal cell accumulation of BP via basolateral membrane
Related to the maximum dose not accumulated dose

Miler Bone 2011
Bisphosphonate Accumulation of Bisphosphonate

Distribution: CKD MBD bone is different…

Uremic low bone turnover
Hyperparathyroidism high turnover state
PTH resistance
Osteomalacia
Glucocorticoid….

Accumulation of Bisphosphonate
Risedronate

- 9 trials: 5mg daily dose
- n=572, CrCL <30 ml/min
- Lateral radiographs
- All normal PTH

New morphometric vertebral fractures at end of trial

Miller JBMR 2005
Renal trial: BMD

- n=31 Haemodialysis patients
- 40mg alendronate weekly for 6 weeks then Outcomes at 6 months
- Excluded:
  - Hi Ca/ P product >5.65
  - Hi PTH > 32 pmol/L
  - poor functional status

No change in BMD - LS, FN, TH

Wetmore Neph 2005
<table>
<thead>
<tr>
<th>Drug</th>
<th>Precaution?</th>
<th>Contra-indication?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate</td>
<td>✓</td>
<td>35</td>
</tr>
<tr>
<td>Risedronate</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Oral Ibandronate</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>IV ibandronate</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Zoledronate</td>
<td></td>
<td>✓ 35</td>
</tr>
</tbody>
</table>
Precaution

• Oral Alendronate not recommended <35ml/min, *due to lack of experience*
• Oral Ibandronate not recommended <30ml/min, *due to lack of experience*
• IV Ibandronate not recommended <30ml/min or creatinine > 200 mcmol/L

Contraindication

• Oral Risedronate contraindicated <30ml/min
• IV Zoledronate contra-indicated <35ml/min (calculated by Cockcroft-Gault)
Bisck study report

- UK primary care records linked to hospital admissions (CPRD/HES)
- Catalonia, Spain linked to Hospital admissions (SIDIAP)
- eGFR < 45 ml/min then oral bisphosphonates user vs non-user
- 3,846 incident BP users vs 15,478 non-users, propensity score matched

Risk of CKD progression: HR 1.18 (1.11, 1.26)

- Previous fracture history: HR 1.36 (1.08, 1.71)

“Our findings should be considered before prescribing bisphosphonates to patients with moderate-to-severe CKD”

Robinson 2020 JBMR
<table>
<thead>
<tr>
<th>Drug</th>
<th>Precaution?</th>
<th>Contra-indication?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate</td>
<td>&lt; 35</td>
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<tr>
<td>Risedronate</td>
<td>✓</td>
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<tr>
<td>Oral Ibandronate</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>IV ibandronate</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Zoledronate</td>
<td>✓</td>
<td>✓&lt;35</td>
</tr>
<tr>
<td>Denosumab</td>
<td>Severe Hypocalcaemia &lt; 30 mL/min or dialysis</td>
<td></td>
</tr>
</tbody>
</table>
48 HD patients (71y, 64% F)
Spine/ Hip fracture or BMD < -2.5SD
iPTH: 6.3 – 25.45 pmol/L
Adjusted Calcium > 2.1 mmol/L
No: cancer, severe liver, heart disease, poor oral

50% cinacalcet, 40% previous fracture

12 month study
Randomised
60mg Dmab 6m vs. IV alendronate (900mcg/monthly) + 0.25 mcg calcitriol +Calcium lactate 1.5g/d
Denosumab in dialysis patients

48 HD patients

No difference in coronary calcification and vascular function

Iseri JBMR 2019
Safety of denosumab in dialysis patients

n = 48 HD patients (71y, 64% F)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Total</th>
<th>Denosumab (n = 22)</th>
<th>Alendronate (n = 24)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypocalcemia (initial 2 weeks)</td>
<td>7</td>
<td>6</td>
<td>1</td>
<td>0.0431</td>
</tr>
<tr>
<td>Hypocalcemia (after 2 weeks)</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0.4783</td>
</tr>
<tr>
<td>Hypercalcemia (initial 2 weeks)</td>
<td>11</td>
<td>2</td>
<td>9</td>
<td>0.0402</td>
</tr>
<tr>
<td>Hyperparathyroidism</td>
<td>13</td>
<td>8</td>
<td>5</td>
<td>0.3304</td>
</tr>
</tbody>
</table>

1= asymptomatic / mild symptoms; 2= requires minimal intervention; 3= hospitalisation; 4= life threatening/ required urgent intervention

+ 0.25 mcg calcitriol + Calcium lactate 1.5g/d + x3/wk dialysis

Iseri JBMR 2019
Dmab and dialysis – CVS risk

- Taiwan
- 21 dialysis (62yr) vs. contemporary non-dmab control (55yr)
- iPTH > 85 pmol/L
- BMD <-2.5
- Single dose of 60mg denosumab
- + calcitriol 0.5 mcg bd + dynamic dialysate calcium
- NO sevelmer, fosrenol, cinacalcet
- 25OHD ~ 68nmol/L

- Baseline and 6 month Coronary calcification scores from CT
Outcome - BMD

(a) Femoral neck

(b) Spine

Denosumab vs Control before and after treatment.
Outcome – Coronary Calcification score

(a) CT Agatston score

(b) CT volume score

Chen OI 2020
Outcome – Digital Calcification score
Calcium carbonate, oral calcitriol, calcium dialysate
8/21 calcium < 2 mmol/L (8 mg/dL)
No cases of symptomatic hypocalcaemia

Chen OI 2020
Anabolic agents:

- Seems counter intuitive
  - CKD is an example of secondary HPTH/PTH resistance

- Role in adynamic bone disease?
  - low turnover state (Post PTx/DM)

- Longer half life (CKD4 (n=5): 5h vs 1.2h)
Anabolic agents:

- Post Marketing study in women (n=1,847)
  - n=30 CKD 4, mean age 80 yrs
  - n=5 CKD 5, mean age 83 yrs
  - 82% secondary fracture prevention

4/33 adverse events – hyperuricaemia, renal dysfunction, injection site warmth
Anabolic agents:

10 Haemodialysis + iPTH < 6.4 pmol/L (60pg/ml)
Age 73 7/10 DM
Treated weekly PTH 56.5 ug
5 untreated
Anabolic agents:

10 Haemodialysis + iPTH < 6.4 pmol/L (60pg/ml)
Treated weekly PTH 56.5 ug
5 untreated

4/10 discontinued
hypotension
malaise

10/22 discontinued

Yamamoto Th Aph & Dial 2020
²Sumida OI 2016
Anabolic agents: hypercalcaemia of adynamic bone disease

51 year old woman with persistent hypercalcaemia despite 3.5 PTx
PTH undetectable
Biopsy proven adynamic bone disease
Anabolic agents: Romosozumab

Phase 1 trial single dose study
8 CKD4, 8 dialysis, 8 healthy

14/24 women, 64.9 years

Adverse events
Injection site reactions 4.2%
Hypocalcaemia n=5 (20.8%)
   nadir day 22
   x1 hospitalization
Increased PTH:
   150% (CKD4); 287% (dialysis)
Reduced phosphate:
   -18% (CKD4); -20% (dialysis)

Bone markers at 15 days

Amgen Clinical study report 2015
Romosozumab is contraindicated in patients with previous myocardial infarction or stroke (see section 4.3).

When determining whether to use romosozumab for an individual patient, consideration should be given to her fracture risk over the next year and her cardiovascular risk based on risk factors (e.g. established cardiovascular disease, hypertension, hyperlipidaemia, diabetes mellitus, smoking, severe renal impairment, age). romosozumab should only be used if the prescriber and patient agree that the benefit outweighs the risk. If a patient experiences a myocardial infarction or stroke during therapy, treatment with romosozumab should be discontinued.
A pragmatic approach

Evenepoel et al. NDT 2021
Case studies 1a Thomas

- Fragility fracture with known progressive renal impairment

Creatinine level, plasma

Estimated GFR, blood

Creatinine clearance vs eGFR if low body weight
Case studies 1a Thomas

- Fragility fracture with known progressive renal impairment

25OHD 14 nmol/L

Risks of replacing vitamin D

- Low vs high dose replacement
- Monitoring serum phosphate

Problem of DXA with high body wt

Trajectory of renal function

Focus on CKD MBD optimisation
Case studies 1b Mary

- Fragility fracture with previously undiagnosed renal impairment
- 86 year old with 2020 wrist fracture
- 2015 metatarsal fracture
- Ht 163 cm
- Wt 54 kg
- Mild cognitive impairment
- eGFR 21
- CrCl 14
Case studies 1b

- Fragility fracture with previously undiagnosed renal impairment
  - 86 year old with 2020 wrist fracture
  - 2015 metatarsal fracture

- Cause of height loss?
  - If multiple vertebral fractures
    - Creatinine improving / stable
    - Phosphate / 25OHD / Calcium
    - PTH <25 pmol/L
  - Supplemental calcium and vitamin D
  - Discuss risk / benefit Dmab with 2 week post dose serum calcium
Case studies 2 Joseph

- Already on Anti-osteoporosis therapy developing renal impairment
- 90 year old male
- 2015 ankle fracture 2016 wrist fracture > EGFR only 30
  - Not for bishosphonatess > start denosumab
Case summary Joseph

2016
Hypocalcaemia
Increase Ca/D supplement to bd

2021 hypocalcaemia
Clinical severity of hypocalcaemia
PPI
25OHD
Taking Ca/D supplements

Start
0.25 mcg alfacalcidol od till calcium normal

Discuss risks vs benefits of Stopping vs pre-dose with alfacalcidol for next injection
• CKD-MBD
• Assessment of bone health in advanced CKD
• Therapeutic approach in patients with advanced CKD presenting with bone fragility/osteoporosis
• Conclusions- take home messages
Conclusions

• Fractures in advanced CKD = high morbidity and mortality
• Balance risks of not treating vs. treatment

• Integrating risk factors/ imaging/ biomarkers/ histomorphometry
• Pragmatic treatment: multilevel, multidisciplinary
  – Optimize CKD MBD, Calcium, Vitamin D
  – Case by case risk/ benefit of anti-osteoporosis medication
European Consensus Statement on the diagnosis and management of osteoporosis in chronic kidney disease stages G4-G5D

Peter Vennoupolos, John Cunningham, Jorge Ferrer, Matthias Haehner, Muhammad Kasim Jassim, Marie-Hélène Lafage-Proust, Daniel Prieto-Alhambra, Pablo Urquina Torres and Jorge Correa-Andrade, on behalf of the European Research Osteoporosis (EROD) workgroup, an initiative of the CKD-MBD working group of the ERA-EDTA, and the Clinical Advisory Board of the National Osteoporosis Foundation, and the National Societies of the IDI

Correspondence to Peter Vennoupolos and Peter Haehner

Objective: To develop management strategies for the prevention of fragility fractures. As such, it aims to stimulate a collaborative approach to the management of osteoporosis in patients with CKD G4-G5D to replace current variations in care and treatment policies.

Keywords: bone mineral density, chronic renal insufficiency, CKD-MBD, minimal bone mass, renal osteodystrophy

SUMMARY OF MAIN RECOMMENDATIONS ON THE DIAGNOSIS AND MANAGEMENT OF OSTEOPOROSIS IN CHRONIC KIDNEY DISEASE G4-G5D

Diagnosis of osteoporosis in chronic kidney disease

1. Osteoporosis is a condition characterized by low bone mass and microarchitectural and qualitative bone deterioration that leads to bone fragility and fracture susceptibility.

2. The operational definition of osteoporosis is based on either a bone mineral density (BMD) assessed by dual-energy X-ray absorptiometry (DXA) at the spine or hip –2.5 standard deviations below the mean in young female adults (T-score).
Q&A
THANK YOU

On behalf of IOF, we thank you for your participation in this webinar
Our vision is a world without fragility fractures, in which healthy mobility is a reality for all.

Join us