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بسم الله الرحمن الرحیم

Management of CKD-MBD

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Introduction

- Patients with stage 4–5 CKD or on dialysis, excluded from RCTs in osteoporosis

- Lack of evidence on fracture prevention in this population

Screening(DXA, VFA)
Case Finding
Multidisciplinary Team

Identify and Treat Secondary Causes
Falls Prevention
Therapeutic Exercises

Optimize Calcium, Protein Intake, Vitamin D Status

Bone Targeted Therapies (Antiresorptive, Anabolic)

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Non-Pharmacological Management

- Identifying and addressing modifiable secondary causes:
  - Smoking
  - Alcohol abuse
  - Glucocorticoids
  - Malnutrition/Underweight
  - Falls risk
  - Lack of physical activity

Exercise

- Physical exercise improving BMD in CKD.

Cardoso et al. BMC Nephrol. 2020
de Araújo et al. Exp Gerontol.2023

- Supervised exercise > Home-based strategies

Hoffmann et al. J Bone Miner Res Off J Am Soc Bone Miner Res. 2022
Watanabe et al. BMC Nephrol. 2021

- Multimodal exercise strategy
  - Resistance
  - Endurance
  - Balance

Cejka et al. Wien Med Wochenschr. 2023

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Calcium
Vitamin D

Calcium/ Vitamin D

- BMD improvements with bisphosphonates in Vit D-replete subjects

+ Sufficient dietary calcium intake

No need for additional calcium supplements

Bourke et et al. Osteoprosis In . 2013

Vitamin D

- Recent large population-based RCTs
  - No evidence of benefit of vitamin D on fracture outcomes

Jorgensen et al. Nephrol Dial Transplant. 2025

Vitamin D

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Jorgensen et al. Nephrol Dial Transplant. 2025

- Correcting vitamin D deficiency prevents BMD loss in kidney transplant recipients

Tsujita et al. J Bone Miner Res. 2022

- No evidence in CKD or dialysis patients

Vitamin D

- KDIGO guidelines recommend:
  - Treating vitamin D deficiency based on 25-hydroxyvitamin D levels

Jorgensen et al. Nephrol Dial Transplant. 2025

Vitamin D

- European consensus statement:
  - Correcting vitamin D deficiency
  - Oral cholecalciferol with once-daily to monthly doses
  - 25-hydroxyvitamin D levels **> 30 ng/mL and < 60 ng/mL**

Jorgensen et al. Nephrol Dial Transplant. 2025

Calcium

- Calcium intake Food or Supplement
- At the levels 2000 to 2500 mg/d

  (The recommended tolerable upper intake range)

- Not associated with CVD risks in generally healthy adults

Chung et al. Ann Intern Med. 2016

Hyperphosphatemia

Hyperphosphatemia

- Hyperphosphatemia ≈ Fracture risk in HD patients

Barrera-Baena et al. Nephrol Dial Transplant. 2024

- KDIGO 2017 recommended to lower serum phosphate towards the normal range.

Hyperphosphatemia

- Dietary changes by limiting phosphorus intake to 800–1000 mg/day

Hyperphosphatemia

- Calcium-containing phosphate binders not recommended.
  - Hypercalcemia
  - Arterial calcification
  - Adynamic bone disease
  - Low PTH

KDIGO 2017. Kidney Int Suppl 2017

Hyperphosphatemia (Non calcium-binders)

- ↓ Serum Ca
- ↓ Coronary artery calcification
- ↓ All Cause mortality
- ↑ Bone Formation Rates

Jamal et al. Nephrol Dial Transplant 2009
Liu et al. Ren Fail 2014

Hyperphosphatemia (Non calcium-binders)

- A novel non calcium-phosphate binder
  Tenapanor

- For constipation-predominant IBS

  – It inhibits the sodium hydrogen exchanger 3 (NHE3) in the bowel
  – Preventing paracellular absorption of phosphate
  (Pathway of phosphate absorption)

Markham et al. Drugs. 2019
King et al. Sci Transl Med 2018
Silva et al. Kidney360 2023

Protein Restriction?

- Sarcopenia is highly prevalent in CKD and especially dialysis patients
- Sarcopenia is associated with osteoporosis in CKD populations
  - Increased protein intake is recommended for sarcopenic older adults

Iuliano et al. BMJ. 2021
Dedeyne et al. Front Nutr. 2021
Paccou et al. J Endocrinol. 2024

Protein Restriction?

Higher protein intake

Benefits > Risks

In older adults with CKD and osteosarcopenia

Gielen et al. Metabolism. 2023

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**Bone Targeted
Therapies
(Antiresorptive,
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Bone Targeted Therapies

- Antiresorptive Agents
  - Bisphosphonates
  - Denosumab
  - SERMs
- Osteoanabolic agents
  - PTH Analogues
    - Teriparatide
    - Abaloparatide
  - Romosozumab

Bone Targeted Therapies

- Stages 1–3 — General population
- Stages 4–5 — Complex and challenging

Bisphosphonates

- For high bone turnover in patients with CKD
- Excretion is mainly through the kidneys
- They accumulate in the setting of CKD

Bisphosphonates

- In GFR < 30 ?
  - Excessive accumulation in the skeleton
  - Over suppression of bone remodeling

Khairallah. Curr Opin Nephrol Hypertens. 2025

Bisphosphonates

- In mild and moderate CKD:
  - Effective
  - Well tolerated
  - Increase in BMD at the hip and lumbar spine
  - Reduction in fractures

Miller et al. J Bone Miner Res 2005
Shigematsu et al. BMC Nephrol. 2017
Whitlock et al. Can J Kidney Health Dis 2024

Bisphosphonates

- IV bisphosphates Acute kidney injury
- Infusion of 5 mg over at least 15 min prevents this complication

Fixen et al. Osteoporos Int. 2022
Miller et al. J Bone Miner Res. 2013

- Slower infusion rates of 30 min in patients with GFR < 50

or

- 60 min < 30 have been recommended

Schini et al. Osteoporos Int. 2022
Sahota et al. Osteoporos Int. 2022

Bisphosphonates

- Off-label use (with proper informed consent):
  - In a personalized approach in patients with stage 4–5 CKD and osteoporosis
  - Consider risks and benefits

Evenepoel et al. Nephrol Dial Transplant. 2021

Denosumab

- Drug metabolism is unaffected by CKD

Denosumab

- In all GFR subgroups showed:
  - Similar, persistent BMD gains
  - Low incidence of fractures

Broadwell et al. J Clin Endocrinol Metab. 2021

Denosumab

- In 324 patients with dialysis and non dialysis-dependent kidney disease:
  - Similar efficacy of denosumab in BMD gain regardless of kidney function

Kunizawa et al. Sci Rep 2020

Denosumab

- The most important adverse effect in CKD patients

Hypocalcemia

- 24% GFR< 15
- 14% In HD

Cowan et al. J Bone Miner Res 2023

Selective Estrogen Receptor Modulators

Selective Estrogen Receptor Modulators

- In a RCT:
- Raloxifene Postmenopausal women
  - With normal kidney function / Stage 1–3 CKD
  - Vertebral fractures ↓

Ishaniet al. J Am Soc Nephrol JASN. 2008

Selective Estrogen Receptor Modulators

- Two small RCTs
  - Raloxifene — Postmenopausal women (Stage 5 CKD)
  - Lower bone turnover
  - Lumbar spine BMD gains

Hernández et al. Kidney Int. 2003
Haghverdi et al. Iran J Kidney Dis. 2014

PTH Analogues

- Teriparatide
- Abaloparatide

PTH Analogues

- Equally effective in patients with stage 3 CKD compared to those with normal kidney function

Laurent et al. Curr Osteoporos Rep. 2025

PTH Analogues

- Adverse events:
  - Transient hypotension
  - Hypercalcemia
  - Hyperuricemia

More common in patients with the lowest levels of GFR

Laurent et al. Curr Osteoporos Rep. 2025

Romosozumab

- Humanized monoclonal antibody
- Against sclerostin (Inhibitor of bone formation)
  - Bone Formation ↑
  - Bone Resorption ↓

Romosozumab

- Similar efficacy and safety in stage 3 CKD patients compared

  to those without CKD

Miller et al. J Bone Miner Res. 2022
Miyauchi et al. J Bone Miner Res. 2022

Romosozumab

- In RCTs:
  - More MI and strokes

    Romosozumab-treated patients than alendronate users

Laurent et al. Curr Osteoporos Rep. 2025

Romosozumab

- Sclerostin suppressed vascular calcifications in CKD?

Brandenburg et al. Nephrol Dial Tranplant. 2019
De Maré et al. J Bone Miner Res. 2022

Osteoanabolic Agents

- Limited evidence to support the efficacy and safety of bone anabolic drugs in CKD stage 4–5 patients.

Thanks For Your Kind Attention