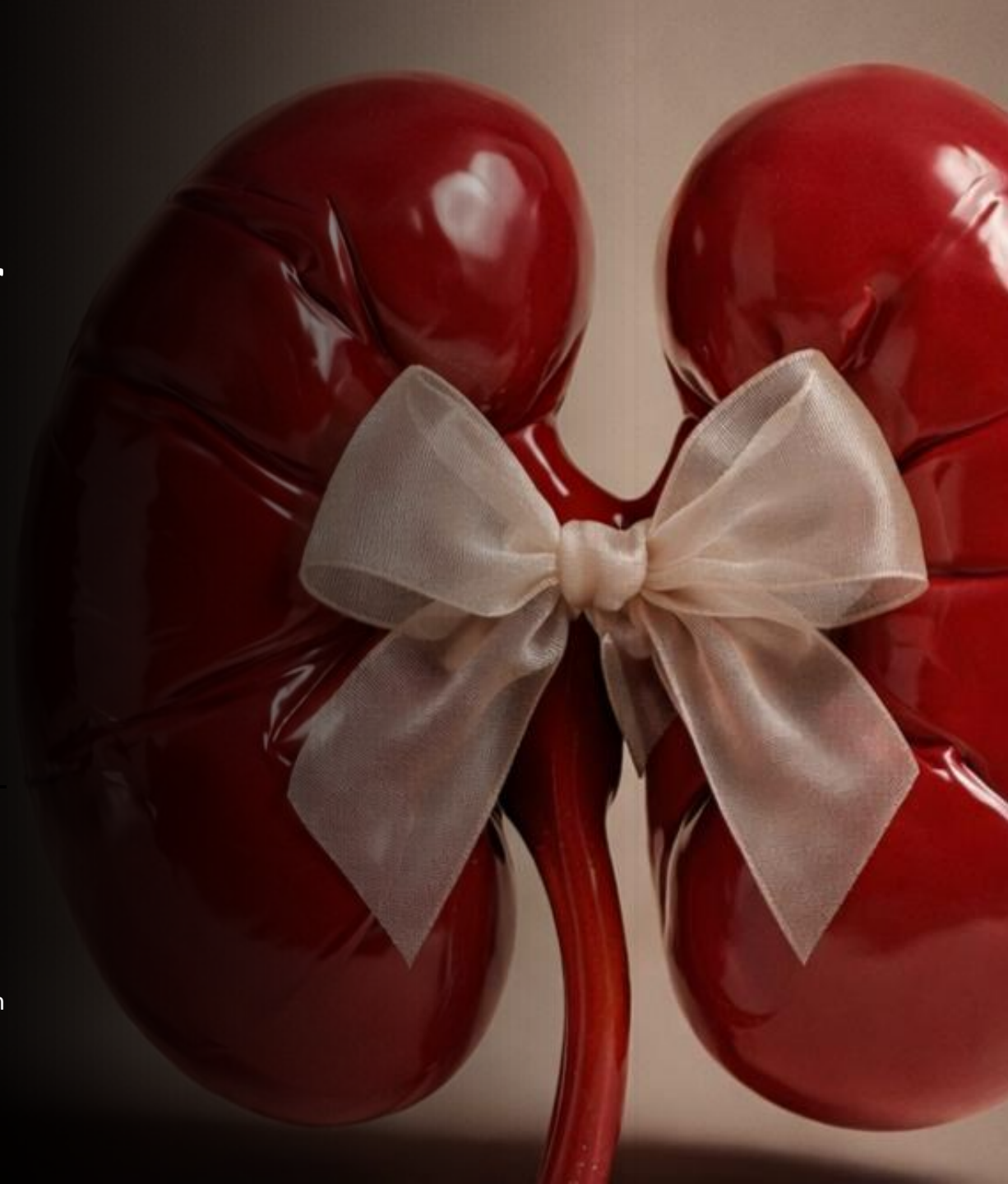
Bone Health After the Gift of Life: Managing Osteoporosis in Kidney Transplant Recipients



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Nephrology & Rheumatology Joint Session

The Clinical Burden

Incidence: Bone loss is most rapid in the first 6–12 months after transplant (up to 10% BMD loss at the spine)

Fracture risk 2–4 times higher than general population, 34% higher than patients remaining on dialysis!

Fractures linked to mortality, graft loss, and disability

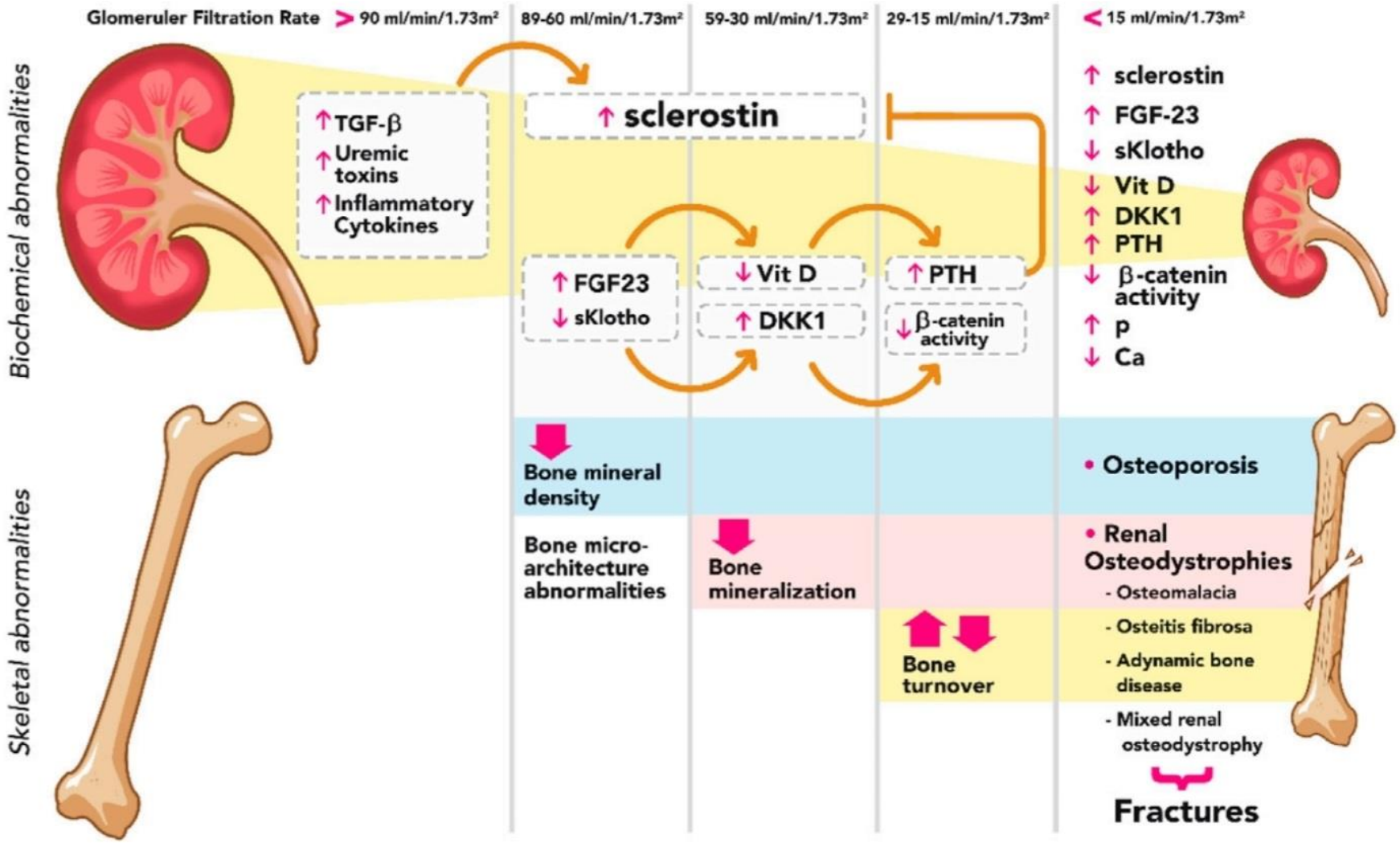
The Paradox: Better survival via transplant leads to longer exposure to fracture risk

Table 1.

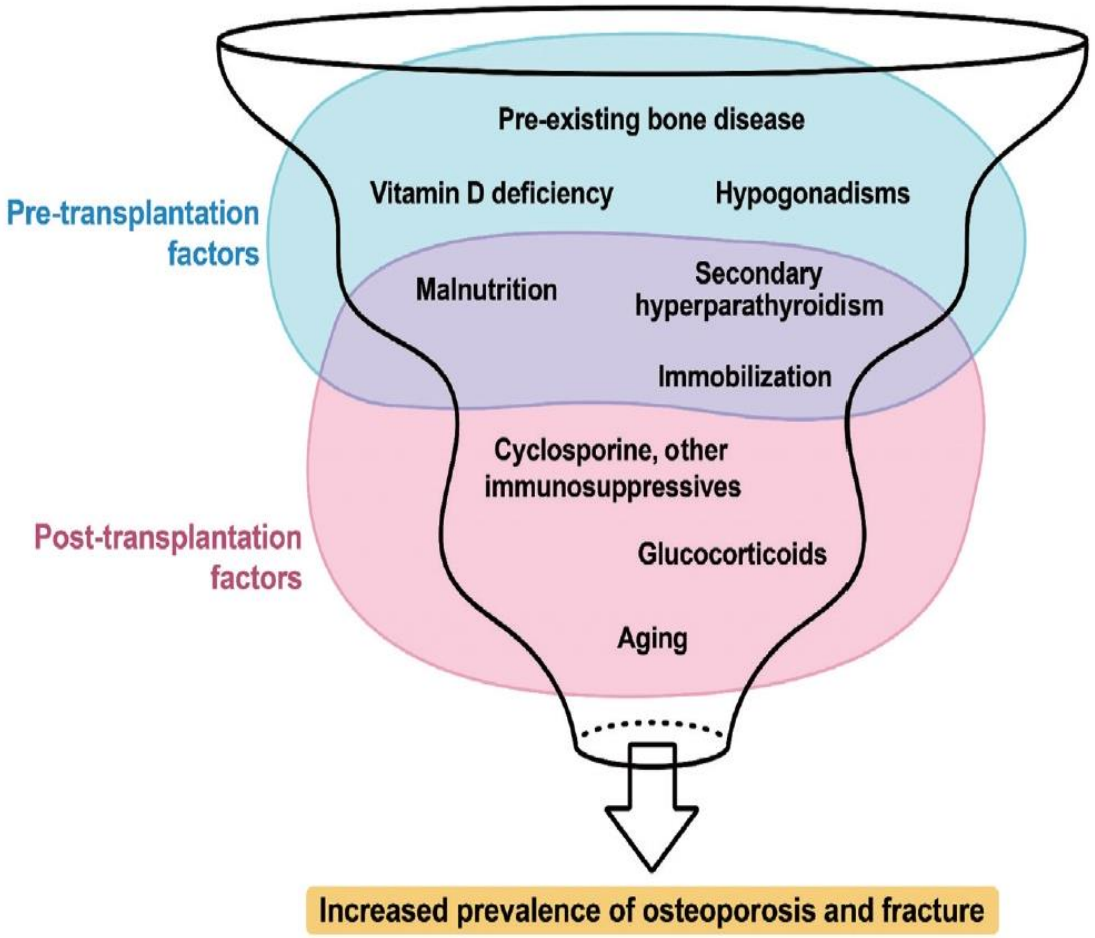
Prevalence of Osteoporosis and Fracture Frequency after Solid Organ Transplantation

Organ transplant type	After transplantation		
	Prevalence of osteoporosis	Prevalence of fracture	Bone loss in the first year
Kidney	Lumbar spine: 17%–49%	Overall: 7%–44%	Lumbar spine: 4%–10%
	Femur neck: 11%–56%		Femur neck: 5%–8%
	Radius: 22%–52%		
Liver	Overall: 46%	Fracture rate: 24%–65%	Lumbar spine: 2%–24%
Heart	Overall: 50%	Vertebral fracture: 33%–36%	Lumbar spine: 6%–10%
			Femur neck: 6%–11%
Lung	Overall: 73%	Fracture rate: 18%–37%	Lumbar spine & Femur neck: 2%–5%

Pathophysiology
Summary diagram of biochemical and skeletal abnormalities in CKD



Pathophysiologic Framework: The “Triple Hit“



Pre-existing: Pre-transplant CKD-MBD (High turnover bone disease or Adynamic bone)

Iatrogenic: Glucocorticoids (GCs) inhibit osteoblasts and trigger osteocyte apoptosis, Cyclosporine

Metabolic: Persistent Hyperparathyroidism (Tertiary HPT) and FGF-23 induced hypophosphatemia

Who Is at Highest Risk?

- Prior fragility fracture (strongest predictor)
- Low pre-transplant BMD
- Older age, female sex
- High cumulative steroid exposure
- Persistent hyperparathyroidism

Guidelines:
KDIGO (2017/2024 Update)

Integration of BMD with CKD-MBD markers

Bone Turnover Markers (BTMs):

- C-telopeptide (CTX) for bone resorption
- Bone Specific Alkaline Phospatase (BSAP) and intact Procollagen type I N-terminal propeptide (PINP) for bone formation

Recommendation: BMD testing is suggested if results will impact treatment (Grade 2C)

Key Insight: Treat the "whole patient“ Correct Ca, PO4, and PTH before labeling as "simple" osteoporosis

Guidelines: ACR (2022) for GIOP

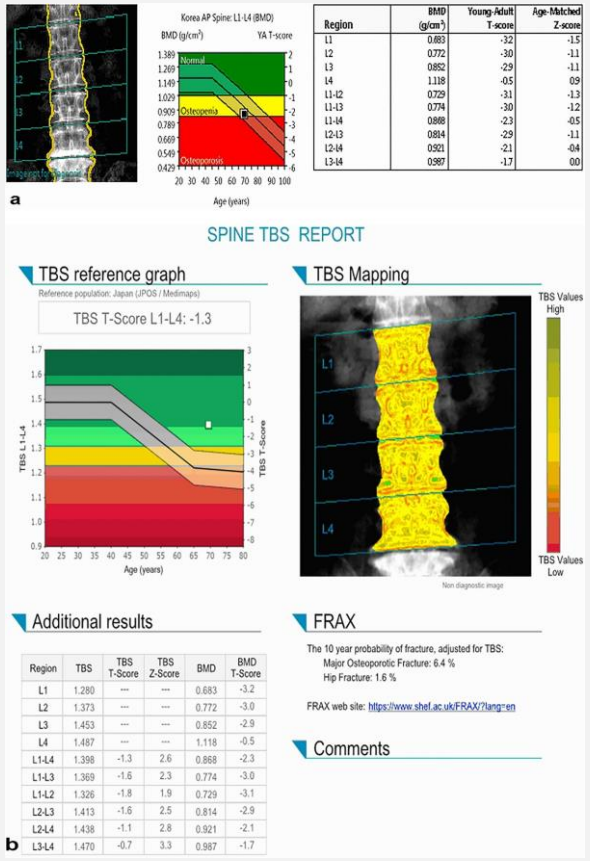
This is where Rheumatologists lead

Threshold: Start prophylaxis if Prednisone ≥ 2.5 mg/day for >3 months in high-risk patients

Note: ACR lacks specific guidance for GFR <30 mL/min, necessitating Nephrologists collaboration

Screening & Diagnosis Challenges

- DXA limitations: Does not distinguish between high and low turnover bone disease
- Trabecular Bone Score (TBS): Mention as a better predictor of fracture risk than BMD alone in KTRs
- The Bone Biopsy: Still the "Gold Standard" but rarely performed. **When should we?**



Clinical Algorithm Early Post Transplant Bone Care

1. **Rheumatology consult**
2. Baseline labs and DXA (pre- or early post-transplant)
3. Correct vitamin D deficiency and optimize calcium intake
4. Assess fracture risk and prior fractures
5. High risk: initiate antiresorptive therapy
6. Low/moderate risk: prevention and close monitoring
7. Reassess at 6–12 months or after rejection therapy

First-Year Post–Kidney Transplant Clinical Management Checklist

(Bone-focused, but integrated into overall care)

PRE-TRANSPLANT or IMMEDIATE POST-TRANSPLANT (0–1 month)

- ◆ Baseline Risk Stratification
- ☐ History of fragility fracture
- ☐ Prior long-term steroid exposure
- ☐ Pre-transplant CKD-MBD phenotype (high vs low turnover)
- ☐ Diabetes, hypogonadism, malnutrition
- ☐ Fall risk assessment

- Baseline Investigations

☐ Serum calcium (corrected)
☐ Phosphate
☐ Alkaline phosphatase
☐ Intact PTH
☐ 25-OH vitamin D
☐ eGFR baseline

First-Year Post–Kidney Transplant Clinical Management Checklist

(Bone-focused, but integrated into overall care)

EARLY POST-TRANSPLANT PHASE (0–3 months)

◆ Universal Preventive Measures (for ALL patients)

☐ Vitamin D repletion (target ≥30 ng/mL)

☐ Calcium intake ~1000–1200 mg/day (diet ± supplement)

☐ Early mobilization & resistance exercise

☐ Fall prevention education

☐ Minimize glucocorticoid dose (protocol-based)

◆ Monitoring

☐ Calcium & phosphate (every 1–2 weeks initially)

☐ PTH trend (not single value)

☐ Watch for hypocalcemia (especially if hungry bone)

First-Year Post–Kidney Transplant Clinical Management Checklist

INTERMEDIATE PHASE (3–6 months)

- Re-assessment
  - ☐ Review fracture risk
  - ☐ Recheck vitamin D and PTH
  - ☐ Evaluate graft function stability
  - ☐ Assess cumulative steroid exposure

- Decide on Pharmacologic TherapyHigh fracture risk (any of the following):
  - ☐ Prior fragility fracture
  - ☐ T-score ≤ −2.5
  - ☐ Rapid bone loss + high steroids

First-Year Post–Kidney Transplant Clinical Management Checklist

LATE FIRST YEAR (6–12 months)

- Persistent Hyperparathyroidism Assessment
- ☐ PTH remains elevated
- ☐ Hypercalcemia present
- ☐ Bone pain or fractures→ Management:
- ☐ Cinacalcet trial
- ☐ Surgical referral if refractory

- Follow-Up Monitoring
- ☐ Calcium, phosphate, ALP every 3–6 months
- ☐ PTH trend
- ☐ Repeat DXA at 12 months (high-risk patients)
- ☐ Review immunosuppression and steroid dose

Approach

Solid organ transplantation recipients

All transplantation recipients

- Ensure adequate calcium intake by consuming 800–1,000 mg daily, prefeably through dietary sources
- Maintain serum 25OHD levels at ≥2–30 ng/mL by administering a daily dose of 800–1,000 IU of cholecalciferol
- Encourage participation in physical activities, particularly resistance exercises

Assessments

- Recommend evaluating bone metabolism, including **BMD**, prefeably **after transplanation**
- Measure **BMD 3 to 6 months** post-transplant if BMD was not assessed before transplantat-
- Recommend monitoring biochemical markers such as Ca, P, alkaline phosphatase, PTH, 25OHD, and bone turnover markers concurrently for a comprehensive assessment
- Consider a referral to **an endocrinologist** if the patient exhibits fracture, rapid bone loss, or has an exceptionally low BMD, indicated by T-score of –3.0 or lower

Candidates for pharmacological intervention

If a post-transplant fracture occurs or osteoporosis is diagnosed, initiate appropriate pharmacological intervention

- Oral bisphosphonate or IV bisphosphonate (especially zoledronic acid)
- Denosumab
- Consider adding calcitriol if there have been recurrences with calcitriol administration

Prevention

The First 90 Days

Steroid Protocols: Early withdrawal vs. low-dose maintenance

Correction of Labs: Aggressive Vitamin D repletion (Target >30 ng/mL), Calcitriol

Electrolytes: Managing "The Renal Leak“ Post-transplant phosphorus wasting

Resistance and weight-bearing exercise (considering patient condition)

Fall prevention strategies

Prevention
Universal
Measures

Calcitriol may help to prevent bone loss during the first year after transplantation and is effective in patients who receive glucocorticoid

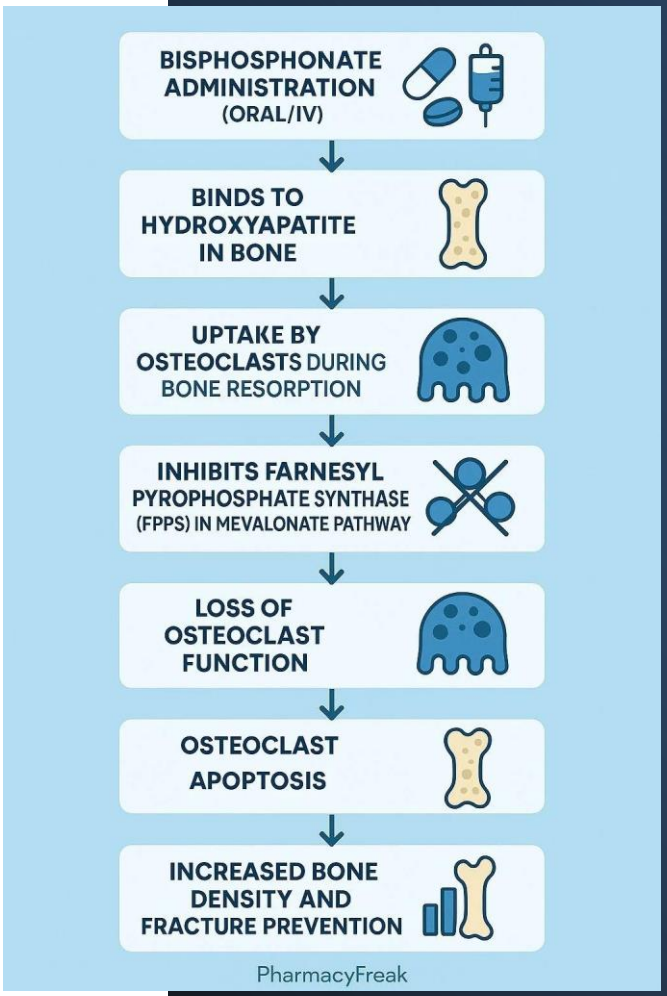
Hypercalcaemia and Hypercalciuria should be monitored

Therapeutic Options

- Bisphosphonates
- Denosumab
- Anabolic therapy (selected cases)
- Management of persistent hyperparathyroidism

Treatment: Bisphosphonates

- Evidence: Smerud et al. (2012): Early Ibandronate preserves BMD
The "Safety Ceiling": Use caution if GFR <35 mL/min
Risk: Potential to exacerbate Adynamic Bone Disease (ABD) if bone turnover is already suppressed
- Fracture data limited but supportive



Treatment: Denosumab

- The Pro: No renal clearance; ideal for Stage 4–5 CKD
- The Study: Bonani et al. (2016) – Significant BMD gain in KTRs
- The Warning: High risk of Hypocalcemia (monitor weekly initially) and the ***Rebound*** Effect (rapid bone loss if doses are delayed)
- Useful when bisphosphonates contraindicated

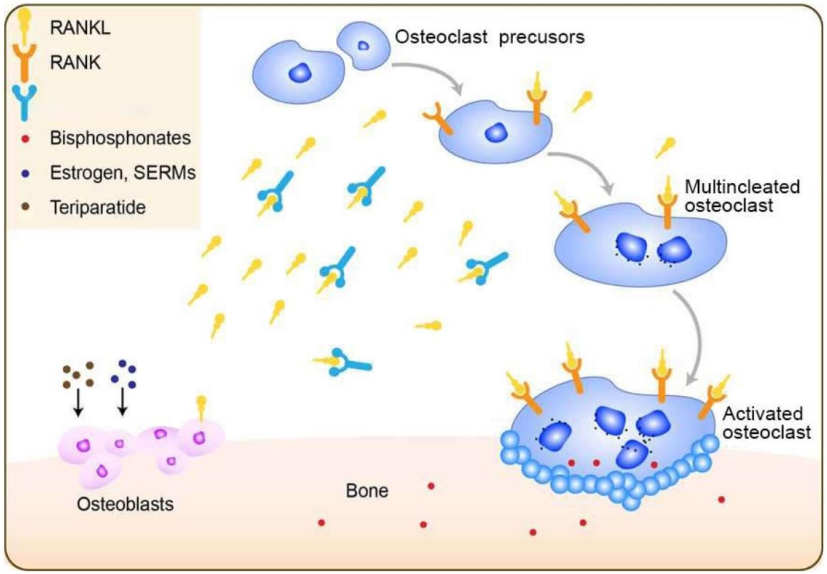
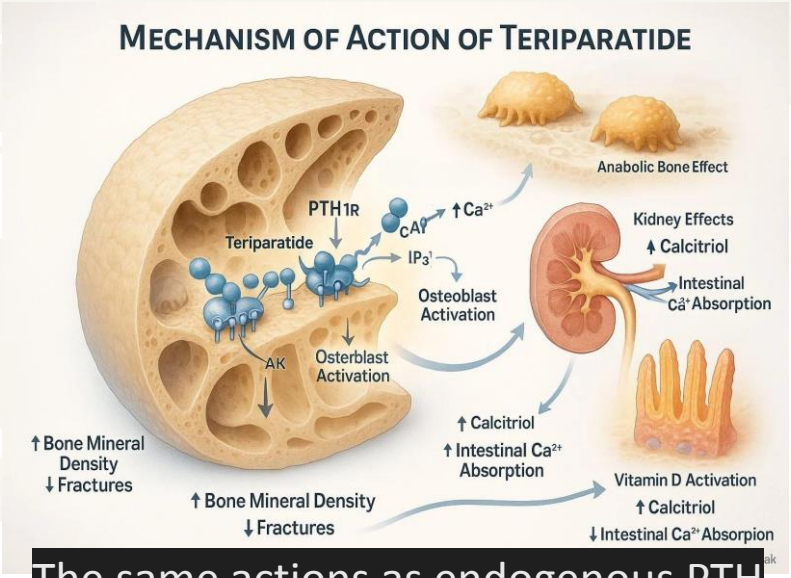


Fig 1. Mechanism of Action of Denosumab

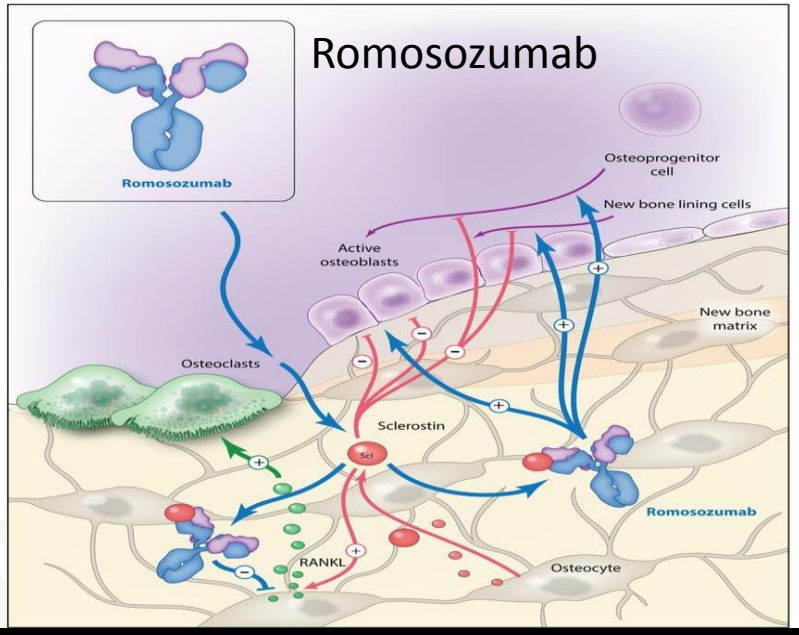
suppresses bone resorption via inhibiting RANK-mediated activation of osteoclasts

The Emerging Role of Anabolics

Teriparatide: May be superior for patients with low-turnover/Adynamic bone
Romosozumab: Recent 2024/2025 data shows massive BMD increases but requires caution regarding cardiovascular risk in high-risk KTRs



The same actions as endogenous PTH



Prevents sclerostin inhibitory effect , the Wnt signaling pathway is activated leading to bone formation

Persistent Hyperparathyroidism

- Present in 30–50% at 1 year
- Cinacalcet for hypercalcemia
- Parathyroidectomy for refractory disease
- Monitor for hungry bone syndrome

Clinical Management

Assessment:

DXA + PTH + Bone-specific ALP

- GFR >35: Oral/IV Bisphosphonates (1st line)
- GFR <35: Denosumab (with Ca monitoring) or Anabolics (if low turnover)
- All: Ensure Vit D sufficiency

Choosing Pharmacologic Therapy

1. Adequate graft function & normal/high turnover → Bisphosphonate

2. Reduced eGFR or bisphosphonate intolerance → Denosumab

3. Suspected adynamic bone disease → Avoid antiresorptives; consider biopsy

4. Severe osteoporosis with low turnover → Consider anabolic therapy

5. Always ensure vitamin D sufficiency and monitoring

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Summary & Takeaways

- Osteoporosis after kidney transplantation is predictable and preventable
- Post-transplant osteoporosis is a multidisciplinary challenge
- The first 12 months are the “Golden Window” for Early assessment and prevention
- Treatment choice must be individualized tailored to the Graft Function (GFR)
- Antiresorptive therapies improve BMD

Controversies & Knowledge Gaps

- Optimal duration of antiresorptive therapy
- Role of bone biopsy in routine practice
- Denosumab discontinuation strategy
- Limited fracture outcome data

Thank You