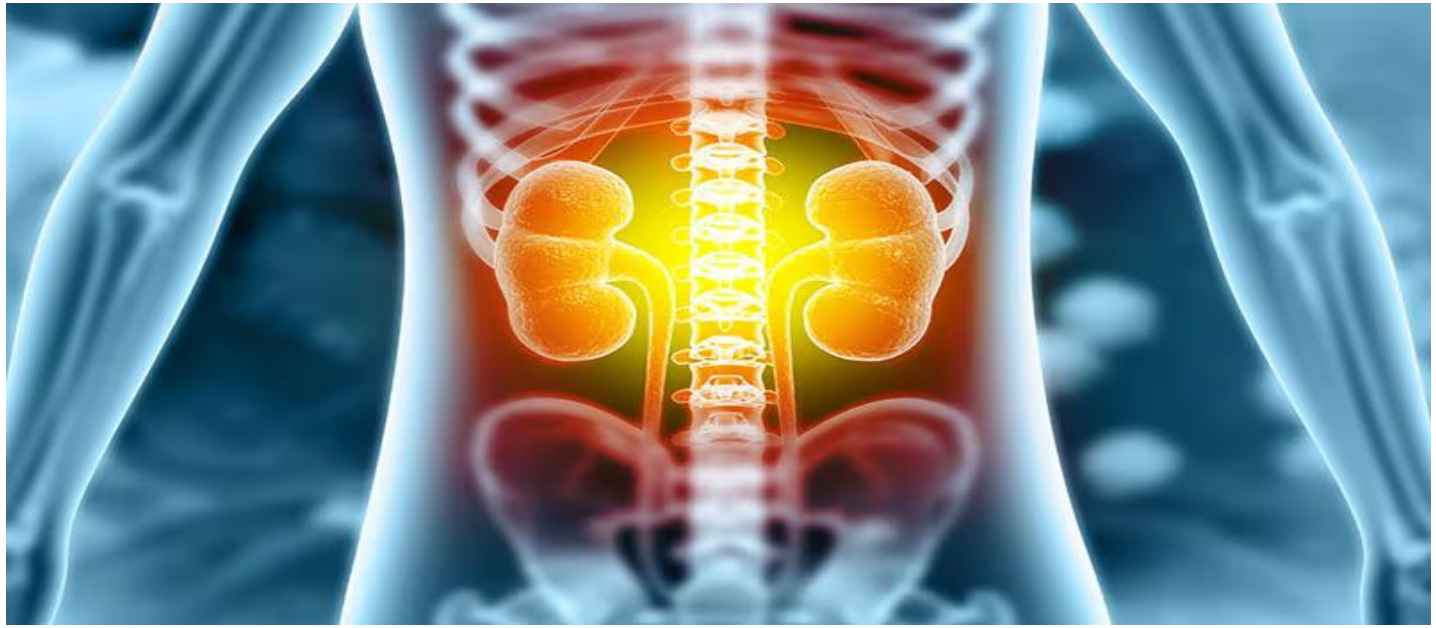
Bone Health Evaluation in a CKD and Post-Transplant Patient: A Case-Based, Question-Driven Approach



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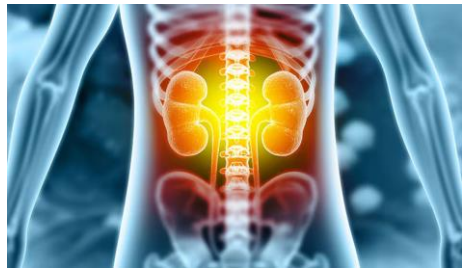
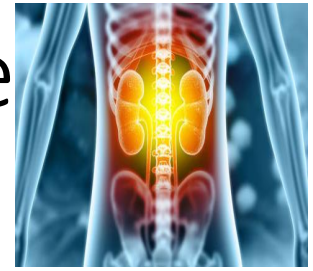
Case Introduction



- 65-year-old male with ADPKD
- Pre-emptive kidney transplant 10 years ago
- Graft loss after recurrent BK virus nephropathy
- On maintenance hemodialysis for 5 years
- Current medications: Prednisolone 5mg/d, Calcium carbonate 500 mg/bid, Sevelamer 800 mg/tds, Valzomix 80-5/d, Pantoprazole 40mg/d, Nephrovit/d
- No active bone pain; physical exam unremarkable
- Family history: **Sister (72-year-old) with renal transplant died from hip fracture after a fall (1 month ago)**
- Patient and family concerned about osteoporosis and fracture risk

How should we systematically evaluate and manage bone health in this high-risk CKD patient with multiple traditional and CKD-related risk factors?

Define the risk profile with the aid of a fracture prediction tool

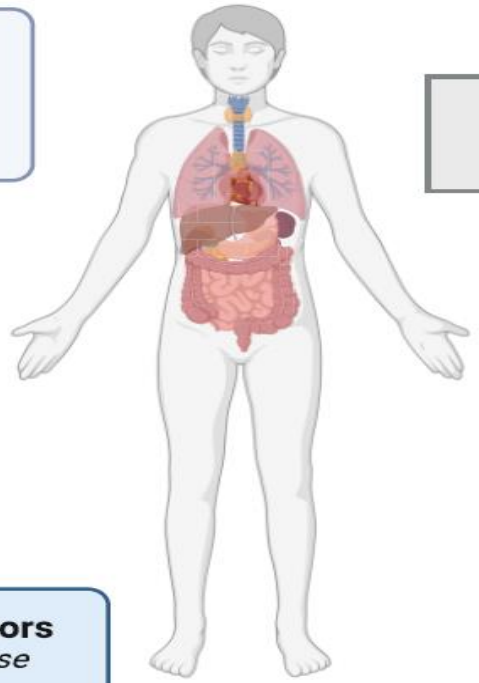


Traditional risk factors
Age-related osteoporosis
LIfe-style (diet, exercise)
Hypogonadism

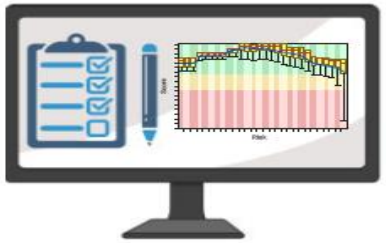
Systemic illness
Cause of CKD
Comorbidities

Polypharmacy
Immunosuppressants
Drugs affecting mineral metabolism
Falls risk

CKD-associated risk factors
Debut and duration of disease
Chronic inflammation
Metabolic acidosis
Mineral metabolism disturbances



Use a fracture risk assessment tool
FRAX, QFracture, Garvan



Take action
Communicate risk
Consider intervention threshold

In CKD patients, fracture risk assessment must integrate clinical factors, CKD-specific abnormalities, and prediction tools—not BMD alone.

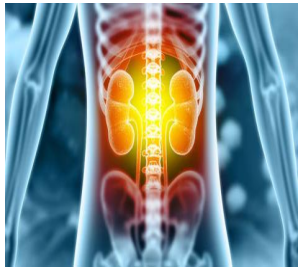
Clinical Risk Stratification: Key Questions

Key Questions for Fracture Risk Assessment

- Prior fragility fractures?
- Family history of major osteoporotic fractures?
- History of falls or imbalance?
- Duration and cumulative dose of glucocorticoids?
- Symptoms suggesting vertebral fracture (height loss, back pain)?
- Physical frailty indicators?

"Physical frailty is a major, often overlooked, determinant of fracture risk—independent of BMD."

Physical Frailty as a Fracture Risk Modifier



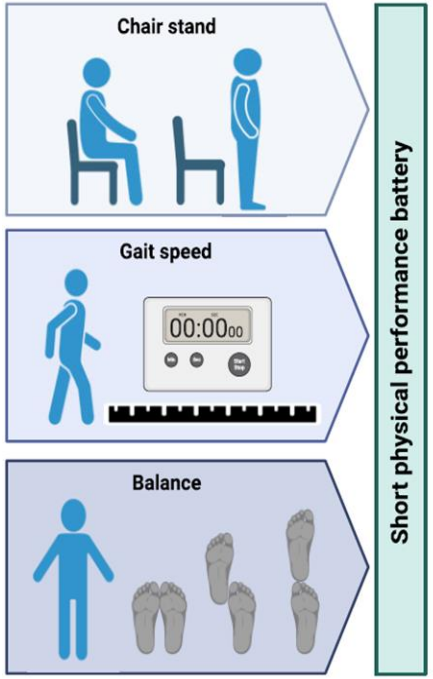
Physical frailty reflects reduced physiologic reserve and impaired resilience to stressors.

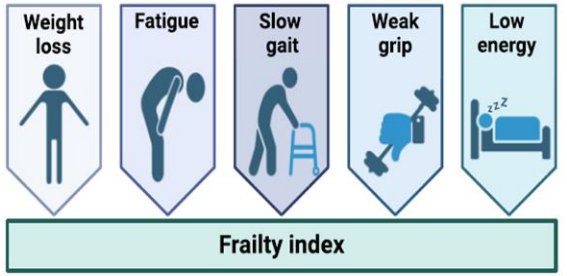
Key features:

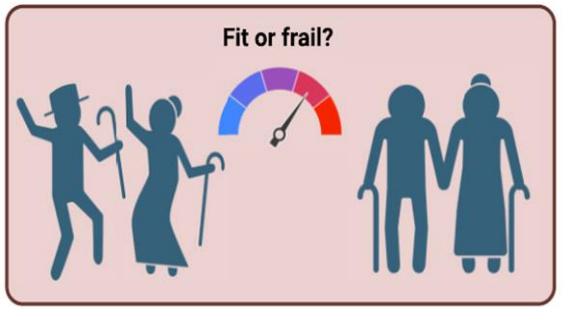
- Slow gait speed
- Muscle weakness
- Exhaustion
- Reduced physical activity
- Impaired balance and falls

Clinical relevance in CKD:

- Strongly associated with falls and fractures
- Predicts fracture risk **independent of BMD**
- Highly prevalent in dialysis and transplant candidates







Implication:

Frailty assessment should complement DXA and fracture risk prediction tools.

Which components of this patient's clinical history place him in the high-risk category before any imaging or labs?"

Risk Factor Mapping

High-risk features (major):

- Age 65→ Reduced osteoblast activity, sarcopenia, falls
- ADPKD → Abnormal bone microarchitecture, lower cortical strength
- CKD G5D→CKD-MBD, low-turnover risk
- Chronic steroids →↓ osteoblasts, ↑ resorption, myopathy
- Long dialysis vintage → Progressive loss of bone quality
- Family history (sister hip fracture death) → Genetic predisposition to fragility
- PPI use→ ↓ Ca absorption, ↑ hip fracture risk
- Calcium carbonate use→ Positive Ca balance → ABD

Intermediate-risk features:

- Post-transplant metabolic bone changes
- Muscle weakness risk
- Reduced mobility

Low-risk features:

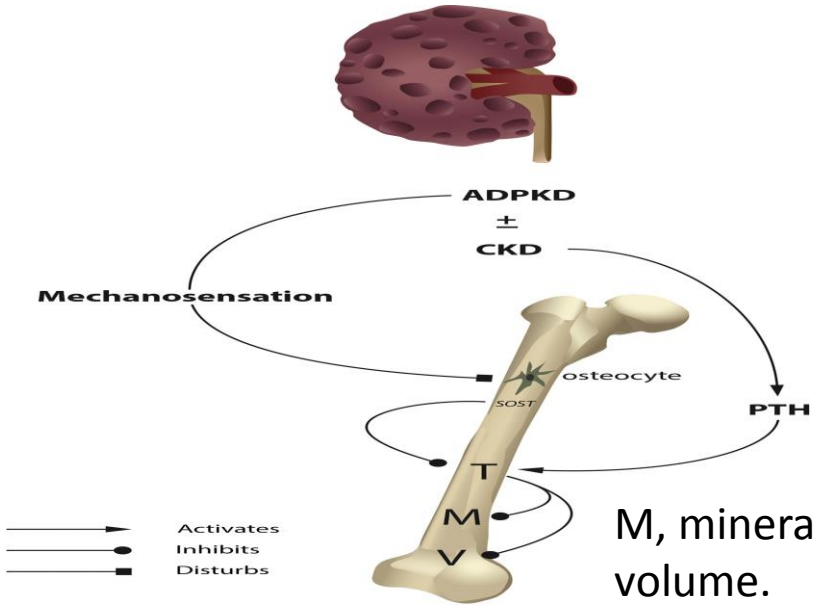
- No diabetes
- No active inflammation

Overall fracture risk: VERY HIGH

What Makes ADPKD Bone Different?

ADPKD-Specific Bone Considerations

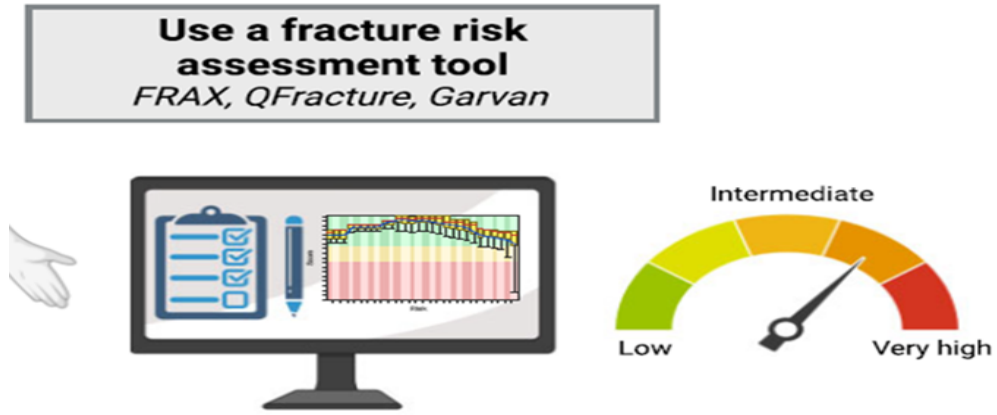
- Altered **cortical bone geometry** independent of eGFR
- PKD-related signaling pathways may impair osteoblast function
- Reduced bone strength not fully explained by BMD
- Fracture risk may be underestimated by DXA alone



M, mineralization; PTH, parathyroid hormone; T, turnover; V, volume.

Fracture Risk Prediction Tools: FRAX vs QFracture vs Garvan

- **FRAX**
  - Guideline-endorsed tool for treatment decisions
  - Estimates 10-year risk of major osteoporotic and hip fractures
  - Does **not** account for falls or CKD-specific bone abnormalities
  - May **underestimate fracture risk** in advanced CKD
- **QFracture**
  - Population-based clinical risk model
  - Includes falls, comorbidities, and medication use
  - Does **not require BMD**
  - Limited validation in CKD and transplant populations
- **Garvan**
  - Incorporates **number of prior fractures and falls**
  - Optional use of BMD
  - Performs well in elderly and high-fall-risk patients
  - Does not include systemic disease or CKD-MBD variables

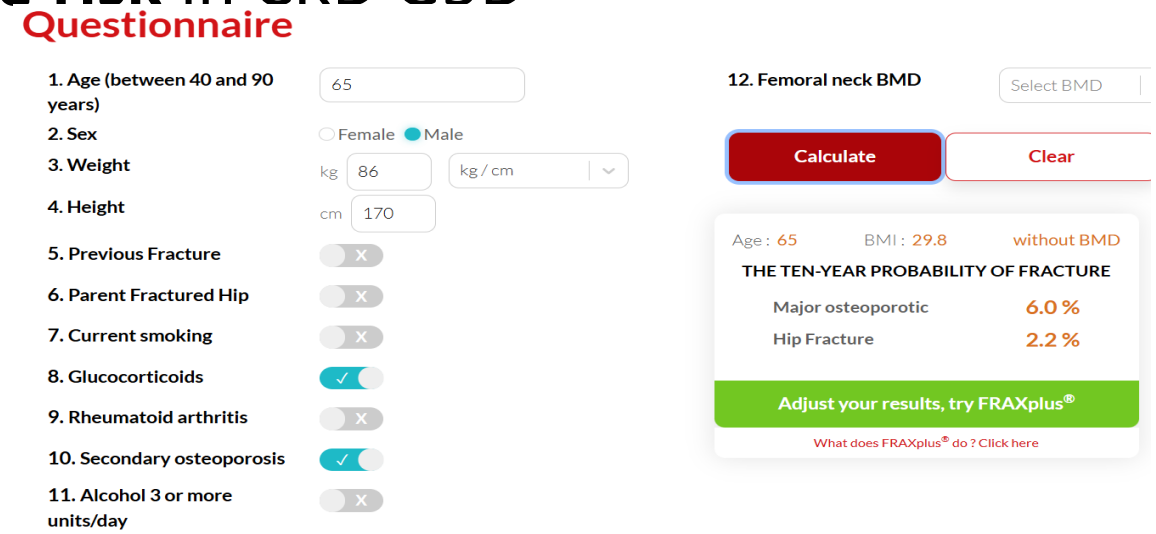


In CKD patients, fracture risk tools complement—but do not replace—clinical judgment and CKD-MBD assessment.

Define Risk with Prediction Tools

Risk Stratification Using Prediction Tools

- FRAX® is **valid but may underestimate risk** in CKD G5D
- Should include:
  - Secondary osteoporosis
  - Parental hip fracture
  - Body weight / BMI
- FRAX does *not* account for:
  - Sarcopenia
  - Frequent falls
  - Muscle weakness
- Vertebral Fracture Assessment (VFA) recommended when feasible



FRAX is a useful starting point, but not the final decision-making tool in CKD patients.

Define Risk with Prediction Tools

Questionnaire

1. Age (between 40 and 90 years) 65
2. Sex Female Male
3. Weight kg 86 kg / cm
4. Height cm 170
5. Previous Fracture X
6. Parent Fractured Hip X
7. Current smoking X
8. Glucocorticoids ✓
9. Rheumatoid arthritis X
10. Secondary osteoporosis ✓
11. Alcohol 3 or more units/day X
12. Femoral neck BMD T-score X -3

Calculate | Clear

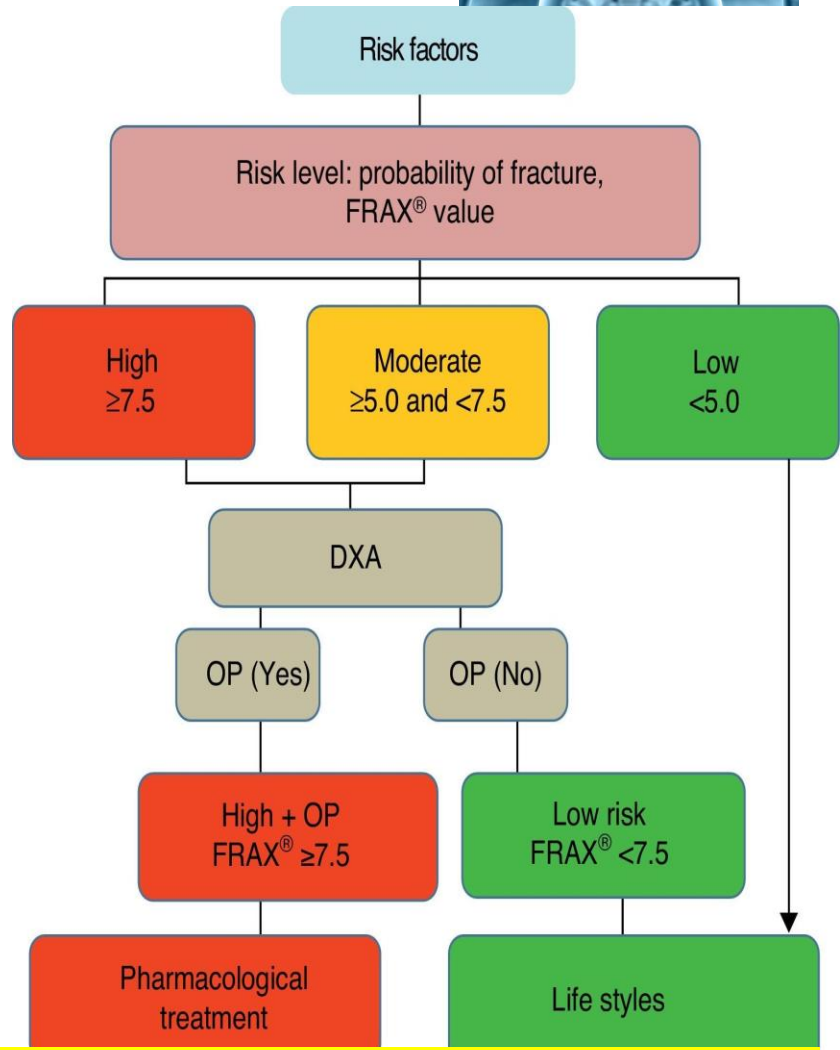
Age : 65 BMI : 29.8 with BMD

THE TEN-YEAR PROBABILITY OF FRACTURE

Major osteoporotic	14 %
Hip Fracture	9.2 %

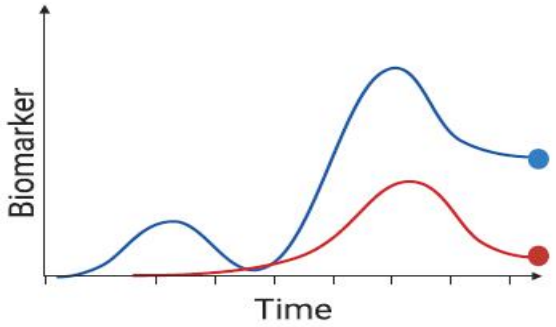
Adjust your results, try FRAXplus®

What does FRAXplus® do ? Click here



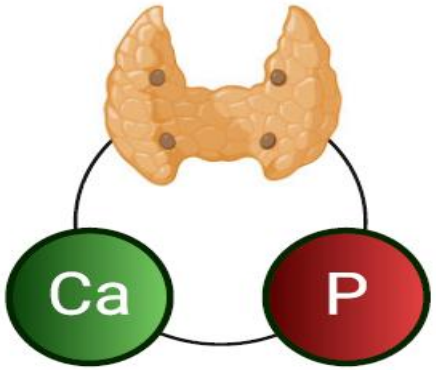
"In CKD G5D, FRAX is best used as a qualitative risk amplifier rather than a treatment threshold tool."

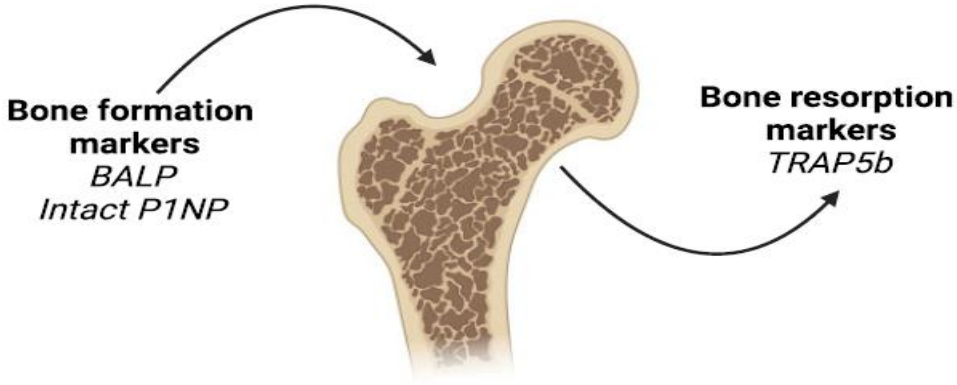
"Before ordering imaging, which laboratory tests are essential to characterize bone turnover in a dialysis patient?"



Biochemical markers of mineral and bone

- *Trends rather than single time points*
- *Consider calcium, phosphorus and PTH together*
- *Add information on vitamin D, acidosis and alkaline phosphatase*
- *Consider novel biomarkers of bone turnover - beware renal clearance*



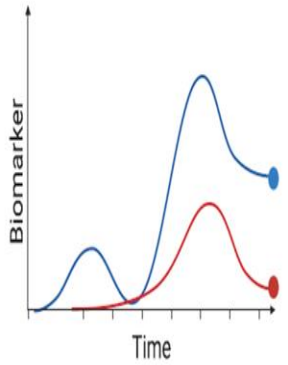


Next Step: What Data Do We Need Now

Initial Data Required for Accurate Risk Profiling

1.Baseline biochemical markers

1. Calcium, phosphate
2. ALP
3. PTH
4. 25(OH)D
5. Serum bicarbonate



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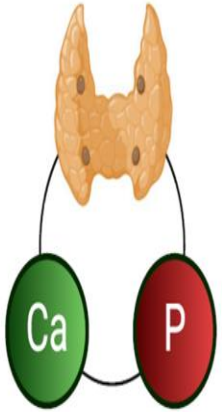
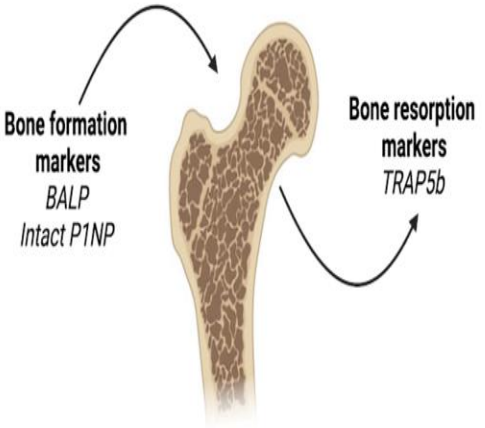
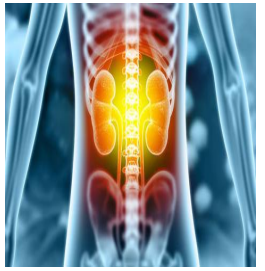
2.Bone turnover markers (CKD-compatible):

1. Bone-specific ALP (BALP)
2. Intact PINP
3. TRAP-5b





Baseline Laboratory Evaluation in CKD G5D Patient



Patient Results:

- **Total Calcium:** 7.9 mg/dL (Albumin 3.5 g/dL) → Corrected Ca ≈ 8.2–8.3 mg/dL (low-normal)
- **Phosphate:** 6.0 mg/dL → **Elevated**
- **PTH:** 450 pg/mL → **Upper target range for dialysis**
- **ALP:** 550 IU/L → **Significantly elevated**
- **Bicarbonate:** 23 mEq/L → Acceptable
- **25(OH)D = 25 ng/mL → Vitamin D insufficiency**

Interpretation:

- High ALP strongly suggests high-turnover bone disease (likely secondary hyperparathyroidism).
- PTH of 450 (with ALP 550) is consistent with active turnover, not adynamic bone disease.
- Hyperphosphatemia indicates inadequate phosphate control → contributes to skeletal and vascular pathology.
- Calcium low-normal despite calcium carbonate + PPI use → possible impaired absorption.
- No evidence of overt metabolic acidosis.
- **Vitamin D insufficiency**
- Insufficient levels may contribute to low-normal calcium and impaired intestinal absorption, especially in the setting of chronic PPI use.
- Adequate vitamin D repletion is essential to reduce the risk of hypocalcemia after antiresorptive therapy.

Calcium & Vitamin D Assessment

Management:

- Initiate nutritional vitamin D repletion:
  - *Cholecalciferol 2000–4000 IU daily* or
  - *50,000 IU weekly for 6–8 weeks*
- Target 25(OH)D ≥ **30 ng/mL** before initiating antiresorptive therapy.
- Avoid excessive calcium supplementation; maintain total intake <800–1000 mg/day.
- Strongly consider discontinuing **pantoprazole** to improve calcium absorption.
- Recheck calcium, phosphate, and PTH after vitamin D repletion.
- Intensify **non–calcium-based phosphate binders** (e.g., sevelamer).
- Avoid increasing calcium-based binders due to vascular calcification risk.
- Reinforce dietary phosphate restriction.

"In dialysis patients, phosphate and vitamin D must be corrected before osteoporosis treatment, but PTH should be optimized—not normalized—to avoid adynamic bone disease."

Recommended Ca intake

- *In children, keep total Ca intake within the age-appropriate normal range.*
- *In adults, ensure a total Ca intake of 800-1000 mg/d and do not exceed 1500 mg/d.*
- *Use online calculators to estimate Ca intake*
- *Include Ca-containing medications*

Recommended Vitamin D levels

- *In children, maintain vitamin D levels >75 nmol/L (30 ng/mL)*
- *In adults, keep vitamin D levels within the recommened range of the background population.*

Biomarkers of Bone Turnover

6. Use CKD-Appropriate Biomarkers to Define Bone Turnover

- Recommended markers:
  - **PTH** (imperfect but useful)
  - **ALP / BALP** (excellent indicator of turnover)
  - **Intact PINP** (formation marker; not cleared by kidney)
  - **TRAP-5b** (resorption marker)
- Avoid:
  - **CTX**, **NTX**, **total PINP** → falsely elevated due to renal clearance.

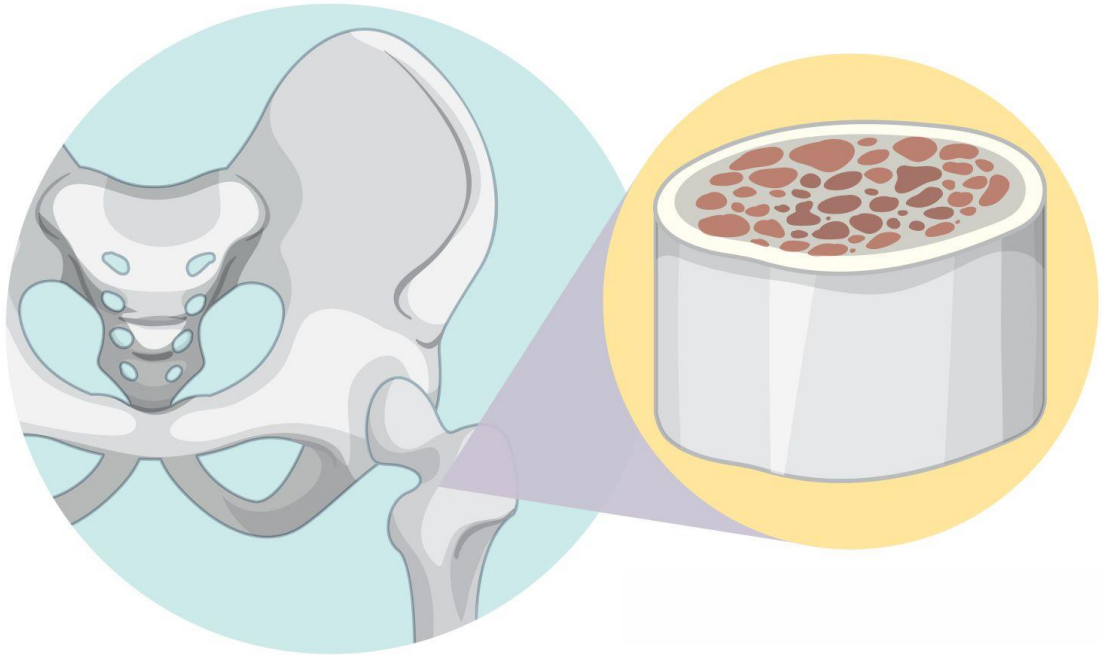
Case Interpretation:

- PTH 450 + ALP 550 → **high-turnover bone disease highly likely**
- A bone biopsy is *not required* at this stage because labs strongly suggest high turnover.

In advanced CKD, osteoporosis treatment should be integrated with CKD-MBD management—neither delayed nor isolated."

Why Bone Biopsy Is Not Required Here?

- Concordant biochemical markers (PTH + ALP)
- Clear high-turnover pattern
- No discordance between labs and imaging
- Biopsy reserved for unexplained fractures or conflicting data



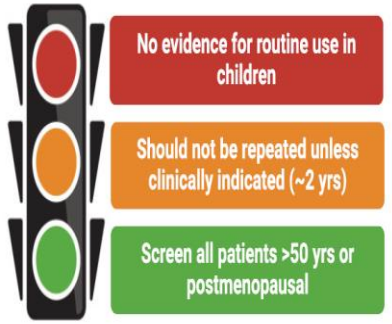
What Are the Next Diagnostic Steps?

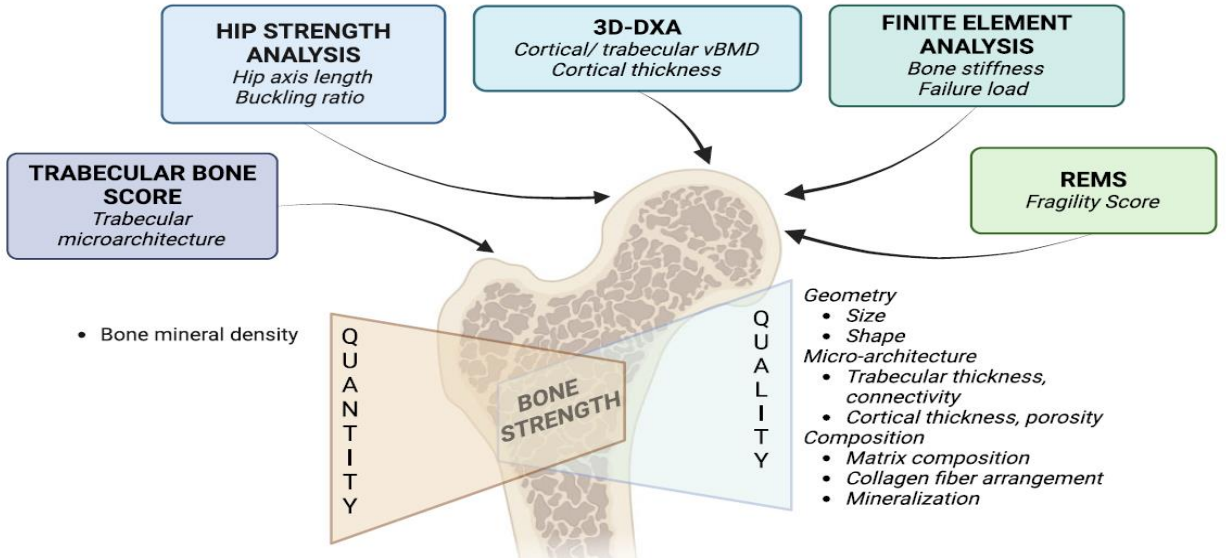
1. DXA scan:

1. Hip (most reliable in CKD)
2. Spine (may be falsely high due to vascular calcification)

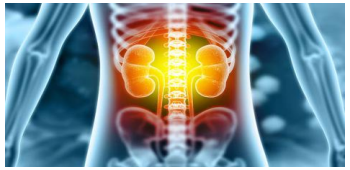
2. Optional:

1. **Trabecular Bone Score (TBS)** for microarchitecture
2. **VFA (vertebral fracture assessment)**
3. Compare with previous transplant-era DXA if available





DEXA Report (Hip & Lumbar Spine)



Site / Parameter	BMD (g/cm²)	T-score	Z-score	Interpretation
Femoral Neck	**0.57**	**−3.0**	−1.4	**Osteoporosis**
Total Hip	**0.68**	**−2.6**	−1.1	**Osteoporosis**
Lumbar Spine (L1–L4)	**1.01**	−1.5	0.0	Osteopenia*
Trabecular Bone Score (TBS)	—	—	—	**1.15 (Degraded)**
VFA (Lateral Spine)	—	—	—	No morphometric fracture

Integrated Interpretation

- **Femoral Neck T-score –3.0** → diagnostic of **osteoporosis**, high fracture risk
- **Total Hip T-score –2.6** → osteoporosis, consistent with cortical thinning typical of CKD
- **Lumbar Spine T-score –1.5** likely **artifactually higher** due to aortic calcification and degenerative spine changes; underestimates severity
- **TBS 1.15 (Degraded)** indicates **severe trabecular deterioration**, often seen in:
  - Long-term CKD
  - Glucocorticoid exposure
  - ADPKD with microarchitectural defects
- VFA: **No morphometric vertebral fractures**, but the absence does not negate elevated fracture risk

Clinical Implications

Based on Labs + DEXA + TBS:

- The patient has **high-turnover bone disease** (high ALP, PTH 450).
- BMD and TBS confirm **structural bone fragility**.
- He is a **very-high fracture risk** dialysis patient.
- This patient meets **diagnostic criteria for osteoporosis** based on hip and femoral neck T-scores.
  Combined with degraded TBS and CKD-specific risk factors, the overall fracture risk is **very high**, even without vertebral fractures.

Treatment decision must consider **turnover status** to avoid adynamic bone disease.

Treatment Strategy Framework

Therapeutic Approach Must Integrate:

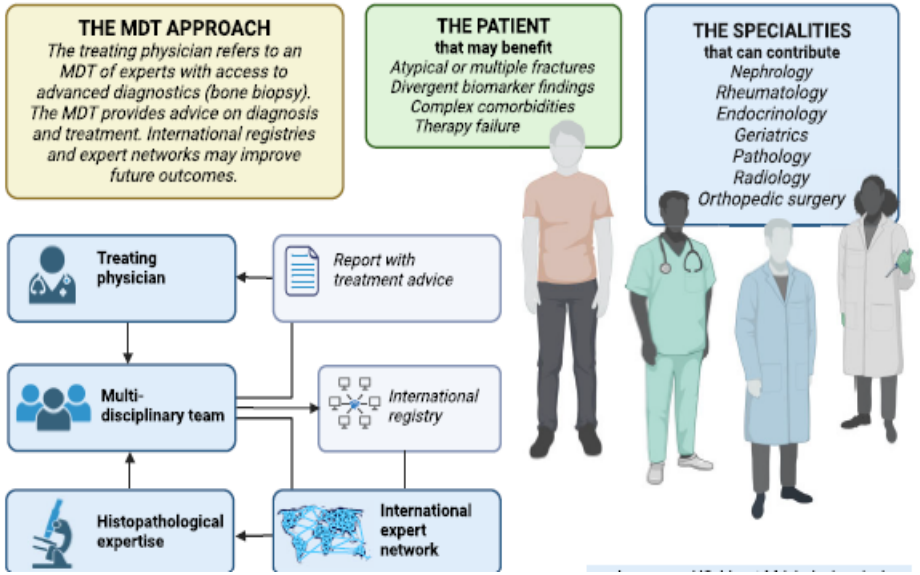
1.Bone turnover status

2.CKD-MBD biochemical control

3.Fracture risk category

4.Life expectancy & dialysis status

5.Transplant candidacy



General Principles:

- Normalize calcium, phosphate, and vitamin D *before* osteoporosis therapy.
- Avoid adynamic bone disease.
- Use agents with evidence in CKD G5D when possible.
- Coordinate care with nephrology/endocrinology/rheumatology.

Additional Non-Pharmacologic Recommendations

Essential Components of Bone Health Management Beyond Medications

- **Exercise program:** resistance + balance training
- **Fall prevention:** home safety evaluation, orthostasis management
- **Nutrition:** adequate protein intake
- **Dialysis adequacy:** Kt/V optimization
- **Treat metabolic acidosis:** keep bicarbonate ≥ 22
- Address frailty: gait speed / handgrip strengthening

Correct Modifiable CKD-MBD Abnormalities

Before Pharmacologic Osteoporosis Therapy:

- Lower serum phosphate to 3.5–5.5 mg/dL
- Reduce or discontinue calcium carbonate (risk: vascular calcification + ABD)
- Optimize sevelamer dose
- Stop PPI (pantoprazole) → improves calcium absorption
- Replete **25(OH) vitamin D**
- Consider low-dose calcitriol if PTH rises after phosphorus control
- Ensure adequate dietary protein to reduce sarcopenia

Which Osteoporosis Medications Are Suitable in CKD G5D with High Turnover?

Why Bone Turnover Matters Before Choosing Osteoporosis Therapy?

- CKD G5D patients can have **high**, **normal**, or **low (adynamic)** bone turnover.
- Anti-resorptives (bisphosphonates/denosumab) may worsen **adynamic bone disease**.
- Anabolics (teriparatide/abaloparatide) may worsen **high-turnover disease**.

- Lab pattern in this patient:
  - **PTH 450 pg/mL → moderately elevated**
  - **ALP 550 IU/L → strongly elevated**
  - **Phosphate 6 mg/dL → uncontrolled**
- → Pattern highly consistent with **high-turnover bone disease**.

This patient is NOT adynamic → antiresorptive therapy can be considered safely.

Pharmacologic Options in This High-Turnover Dialysis Patient

✓ **1. Denosumab (Preferred in CKD G5D)**

- Not renally cleared
- Effective at increasing BMD and reducing fractures
- Can be used in dialysis patients
- **Risk:** hypocalcemia → must correct Ca, Vit D first

✓ **2. Bisphosphonates (Use with caution)**

- Accumulate in bone; long half-life
- Limited evidence in dialysis
- Risk of adynamic bone disease is **low when turnover is high**
- Consider **alendronate** or **ibandronate** if denosumab unsuitable

❌ **Not Recommended in High Turnover:**

- **Teriparatide / abaloparatide**
  (Anabolics worsen high-turnover and hyper-PTH state)

❌ **Avoid:**

- Romosozumab → limited data in dialysis; risk of vascular calcification

Selecting the Best Drug for This Patient

Why Denosumab Is the Optimal Choice Here:

- High fracture risk + severe osteoporosis
- High bone turnover (ALP 550, PTH 450) → safe to use antiresorptive
- Denosumab has evidence in **dialysis patients**
- Faster reduction of bone resorption compared to bisphosphonates
- No risk of accumulation
- Convenient 6-monthly injection
- Works even when BMD is low + TBS degraded

Monitoring Required:

- Check Ca, P, ALP, PTH 7–10 days after injection
- Ensure vitamin D level > 30 ng/mL
- Calcium supplementation *only if needed*, avoid excess

Follow-Up & Monitoring Plan

3–6 Month Follow-Up:

- Serum Ca, P, ALP, PTH
- Vitamin D
- Assess muscle strength & fall risk
- Check for hypocalcemia post-denosumab
- Adjust binders and dialysate calcium if needed

12–24 Month Follow-Up:

- Repeat DXA hip ± TBS
- Evaluate fracture status and treatment response
- Reassess turnover (PTH + ALP trends)

Follow-Up at 3 Months

3-Month Follow-Up Findings:

✓Corrected Ca: **8.4 mg/dL**

✓Phosphate: **4.5 mg/dL**

✓ALP: **300 IU/L** (down from 550 → –45%)

✓PTH: **320 pg/mL**

- Serum calcium stable
- Phosphate improved with reinforced sevelamer adherence
- PTH decreased moderately (expected)
- ALP trend declining, suggesting reduction in turnover
- No new falls or fractures reported
- Physical performance: improved gait speed, stable grip strength

Treatment response is appropriate; no biochemical signal of adynamic bone disease.

Continue current therapy and monitoring.

Follow-Up at 6 Months

6-Month Follow-Up:

✓Corrected Ca: **8.7 mg/dL**

✓Phosphate: **4.6 mg/dL**

✓ALP: **260 IU/L**

✓PTH: **290 pg/mL**

✓25-OH D: **34 ng/mL**

- Received second denosumab dose
- Calcium and vitamin D remained adequate
- Phosphate within acceptable limits
- ALP significantly improved
- PTH trending slightly lower but not suppressed
- Patient reports better functional mobility, no back pain or height loss
- No signs of hypocalcemia after second dose

The patient shows **biochemical improvement** and **clinical stabilization** of bone health. He remains high-risk but is responding appropriately to therapy.

New Clinical Decision: Candidate for Repeat Kidney Transplant

Clinical Update at 6 Months:

The patient has now decided to pursue **a second kidney transplantation**. Bone health evaluation must be re-assessed as part of the **pre-transplant workup**.

Key Questions:

- How should ongoing osteoporosis therapy be managed now?
- What additional assessments are required before transplantation?
- Are modifications needed due to upcoming immunosuppression?

Pre-Transplant Bone Health Re-Evaluation (Post-Treatment)

At the Time of Pre-Transplant Assessment:

1.Biochemical Re-Assessment:

1. Calcium stable
2. Phosphate better controlled
3. ALP trending downward
4. PTH moderate (not suppressed)
5. Vitamin D repleted

2.Treatment Response:

1. Denosumab tolerated well
2. No oversuppression of turnover
3. No hypocalcemia episodes

3.Clinical Status:

1. No fractures
2. Improved mobility
3. Reduced frailty markers

The patient enters the transplant evaluation phase with **stabilized bone turnover**, reduced risk of post-transplant hypocalcemia, and improved structural bone health.

What Additional Bone Assessment Is Needed Before Transplant?

Pre-Transplant Bone Workup Includes:

- Updated labs: Ca, P, ALP, PTH, 25(OH)D, bicarbonate
- Verification of stable turnover (PTH 200–500 acceptable)
- Medication review (ensure no calcium overload)
- Fall risk evaluation
- Consider **repeat DXA only if >12 months old**
- No need for bone biopsy due to:
  - High-turnover pattern
  - Good response to therapy
  - Stable biomarker trends

Managing Denosumab in a Transplant Candidate

How Denosumab Influences Pre-Transplant Planning:

- Safe to continue **before transplant**
- Must anticipate risk of **post-transplant hypocalcemia** when PTH rapidly declines
- Ensure:
  - Vitamin D sufficiency
  - Calcium monitoring immediately post-transplant
  - Avoid excessive calcium loading before surgery
- Coordinate with transplant team regarding timing of the next dose

Plan:

- Continue current dosing schedule
- Increase monitoring frequency during the peri-transplant period
- Maintain phosphate control to avoid post-op hypocalcemia

Final Summary of Follow-Up and Pre-Transplant Bone Management

- Osteoporosis therapy initiated **while on dialysis** due to very-high fracture risk.
- Follow-up at 3 and 6 months showed:
  - Stable calcium
  - Improved phosphate control
  - Declining ALP
  - No signs of adynamic bone disease
- Patient became a **candidate for re-transplantation** at 6 months.
- Pre-transplant workup confirms **stable bone turnover and adequate vitamin D**, allowing continuation of denosumab.
- Patient is now optimally prepared for the **early post-transplant high-risk window** when rapid bone loss typically occurs.

Peri-operative Course:

- **Day 0 (pre-op):** Corrected Ca **8.6 mg/dL**, P **4.1 mg/dL**, PTH **260 pg/mL**
- **Day 1 post-op:** Ca **8.0 mg/dL** (mild fall), PTH **150 pg/mL**
- **Day 2 post-op:** Ca **7.6 mg/dL** → patient reports mild perioral numbness
  - **Action:** start oral calcium carbonate 1000 mg TID + calcitriol 0.25 µg BID; check Ca q12–24h
- **Day 5 post-op:** Ca **8.0 mg/dL**, symptoms resolved; continue oral supplements and taper per Ca trend
- **2 weeks post-op:** Ca **8.3 mg/dL**, PTH **95 pg/mL** (expected decline), ALP **220 IU/L**

Interpretation:

- Rapid fall of PTH post-transplant is expected and contributed to transient hypocalcemia, potentiated by prior denosumab (antiresorptive effect). Early detection allowed prompt oral therapy and avoided IV calcium
- **Action going forward:**
- Continue Ca monitoring until stable >7–10 days.
- Reassess timing of next denosumab dose
- consider delaying additional antiresorptive until PTH and Ca stabilized and MDT discussion completed.

Post-Transplant Follow-Up (1–12 months)

- **First month:** daily → q48h Ca checks until stable; monitor symptoms.
- **1–3 months:** Ca, P, PTH weekly → monthly as stabilizes; check ALP monthly.
- **6–12 months:** repeat DXA at 12 months if clinically indicated; reassess fracture risk and need for continued antiresorptive therapy.
- **If persistent hypocalcemia or very low PTH (<50 pg/mL)** → endocrinology consult; consider holding further denosumab.
- **If stable Ca/PTH and no fractures** → plan MDT decision on continuation of antiresorptive vs switching to alternative agent.

pre-transplant denosumab reduces early post-transplant bone loss risk but mandates **proactive peri-op Ca surveillance** and MDT coordination.

Lessons from This Case

- DXA alone is insufficient in CKD
- Bone turnover defines safe therapy
- Treat osteoporosis and CKD-MBD **together**, not sequentially
- ADPKD adds a layer of hidden skeletal fragility
- Pre-transplant bone optimization changes post-transplant outcomes

Bone Health Across the CKD–Transplant Continuum

Thank you for your attention

Questions & Discussion

Bone Disease in CKD requires early recognition, integrated management, and multidisciplinary care—before and after transplantation.