

Update: Osteoporosis & The Solid Organ Transplant Patient

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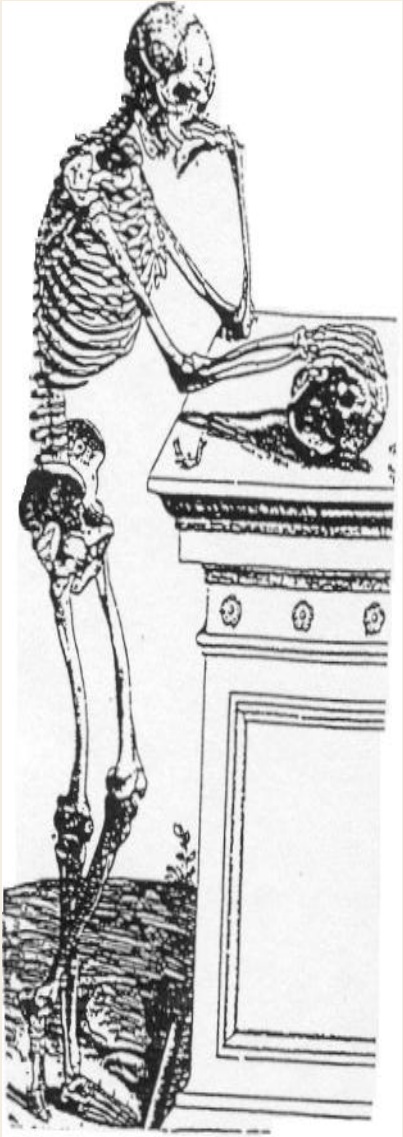
BT Disclosures

Research :

Research Support: Amgen

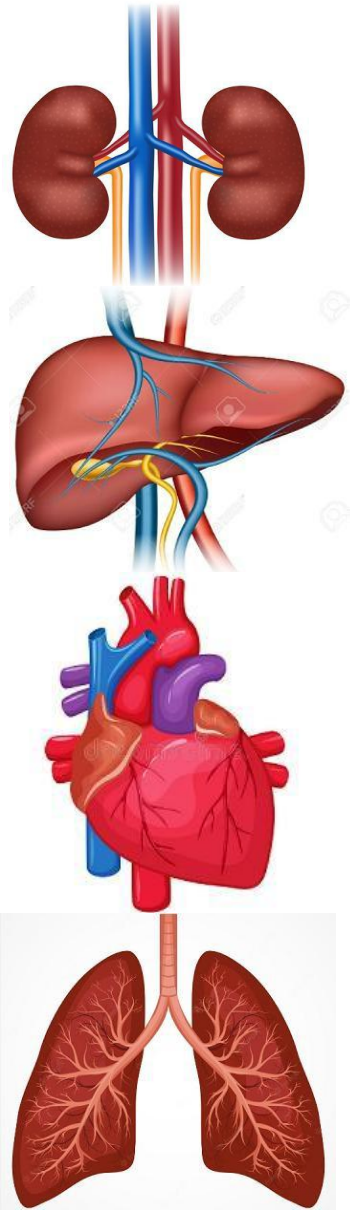
Advisory Panel: Kyowa Kirin

Agenda



Why are you thinking about bone?

1. Osteoporosis overview
2. DXA Bone density testing
3. Labs
4. Medications & Management
5. Cases & Organ Specific issues
6. Take home points



2025 Organ Transplants in US:

49,064 transplants, deceased & living donors

Kidney : 27,573

Liver :12,344

Heart: 4,587

Lung: 3,490

Pancreas w/w-out kidney: 911

110,113 on the wait list, mostly kidney

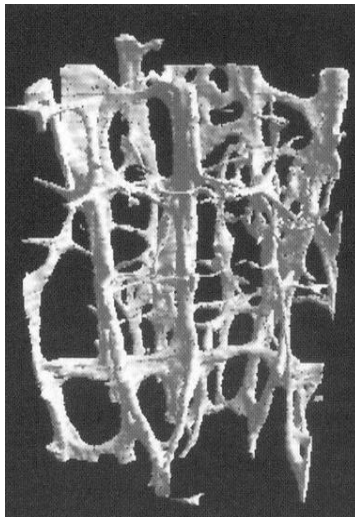
VUMC 960 total t'plants in 2025

Defining Osteoporosis:

Most common metabolic bone disease in adults



Normal Bone



Osteoporotic Bone

1. **Functional definition**: A systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture.¹
2. **Quantitative Definition**: WHO T-score ≤ -2.5
3. **Fracture Risk Definition**: FRAX $\geq 20\%$ major fracture risk, or $\geq 3\%$ hip fracture risk
4. **Presence of fractures**:

Hip fracture (regardless of DXA findings)

Clinical vertebral, proximal humerus or pelvis fx with osteopenia

¹Consensus Development Conference: Diagnosis, Prophylaxis, and Treatment of Osteoporosis. *Am J Med* 1991;90:107-110

² Kanis JBMR 1994

Siris, et. al., Osteoporos Int, 2014: 25; 14391443

Hip Fracture: Devastating Event

Mortality rate comparable to breast cancer
and prostate cancer

20% excess mortality in the first year

50% incapacitation

20% of females need assisted living or
nursing home

80% of 75 yo preferred death to hip fx &
nsg hm



- Cooper C, et al. Am J Epidemiol. 1993;137:1001
- Vincent G, et al. JBMR Plus. 2024 Apr 9;8(5)

Hip Fracture: Devastating Toll: "The 4 Ds"

1. **Death**^{2,6}

Mortality rate same as breast and prostate cancer

2. **Disability**^{1,2}

50% incapacitation

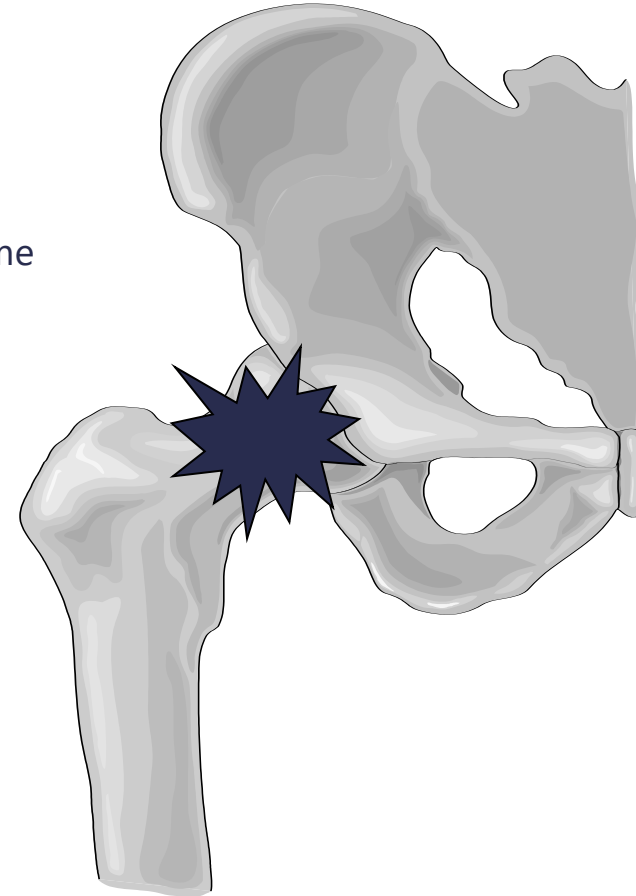
3. **Dependence**^{1,2}

20% of females need assisted living or nursing home

4. **Delirium & dementia**^{3,4,5}

40% to 60% risk of delirium

41% higher rate of dementia



¹www.share.iofbonehealth.org/WOD/2012

²Cooper C, et. al., Am J Epidemiol 1993;137:1001

³Gustafson et al. . J Am Geriatr Soc 1988;36:525–530.

³Givens et al J Am Geriatr Soc. 2008 Jun;56(6):1075-9

⁴Tsai C et al, Medicine 2014 93(26) :1-7

⁵Marcantonio et al J Am Geriatr Soc. 2011 Nov;59 Suppl 2:S282-8

⁶Panula et al BMC Musculoskeletal Disorders 2011, 12:105

Previous Fractures Are Important !

Previous fracture: 2 X your risk of another fracture

“Imminent Fracture Risk”:

Highest within the first 12 - 24 months after the initial fracture

Spine fractures create the most dramatic risk escalation:
single spine fracture increases risk by 2.5 to 4X

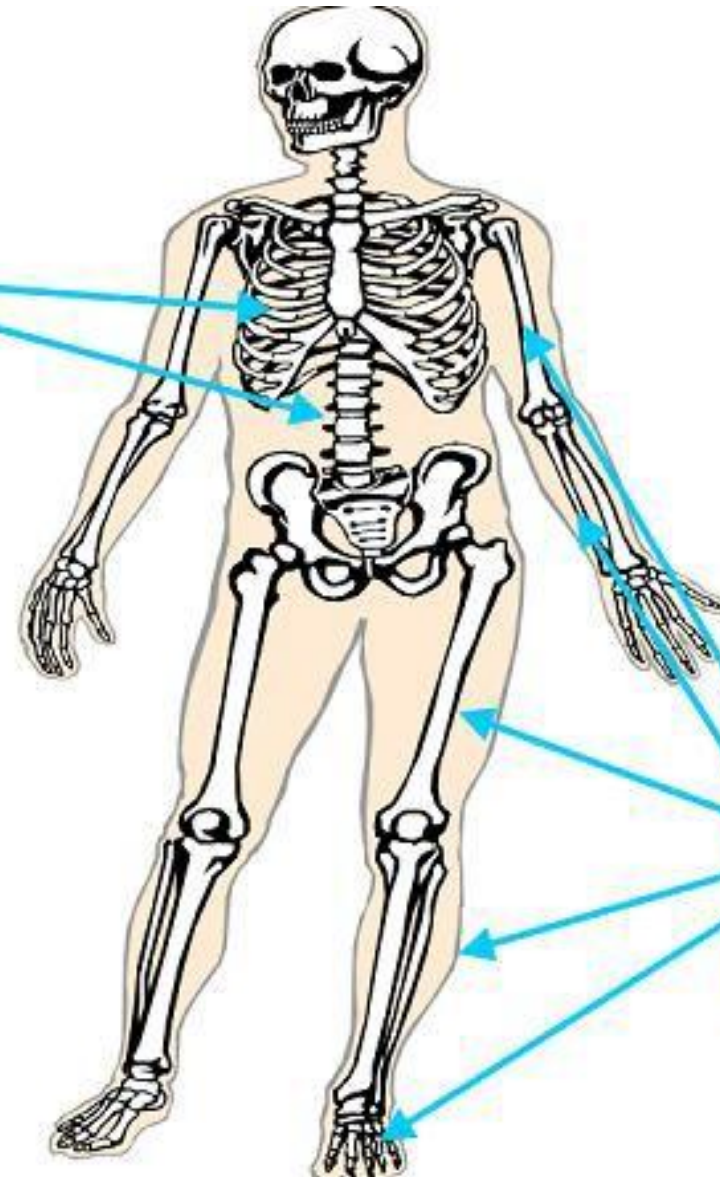


Osteoporosis & Fracture After Transplant

Organ	Osteoporosis Prevalence	Fracture Prevalence or Rate	First Year Bone Loss
Kidney	Lumbar spine 17%-49% Femoral Neck 11%-56% Radius 22%-52%	7%-44% prevalence	Lumbar spine 4%-10% Femoral neck 5%-8%
Liver	46% overall	24%-65% rate	Lumbar spine 2%-24%
Heart	50% overall	Vertebral 33%-36% prevalence	Lumbar spine 6%-10% Femoral neck 6%-11%
Lung	73% overall	18%-37% rate	Lumbar spine & Femoral neck 2%-5%

Specific Organ Transplant & Localization of fractures

Common after lung, cardiac and liver transplantations



Common after kidney transplantation

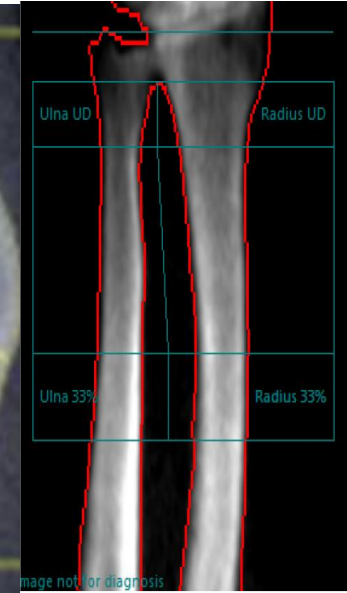
When should DXA Bone Density testing be performed?



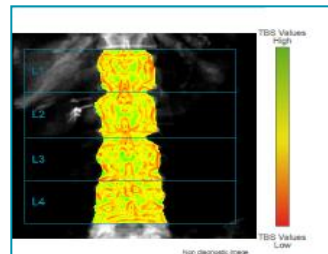
Lumbar Spine



Femoral Neck
Total Hip



33% Radius



Trabecular Bone Score

Medicare Will Reimburse for DXA Bone Density Testing

1997 Bone Mass Measurement Act

1. Women with estrogen deficiency (E28.39)*
2. Spine x-ray evidence of fracture or OP (M48.54XA)*
- 3. Glucocorticoid therapy (3mos, 5 mg/d) (Z79.52)***
4. Primary Hyper-PTH (E21.0)*
5. Follow-up OP treatment (23 months unless medical reason for **sooner e.g. steroids**) (M81.0)*

**Note: ICD 10 codes are examples and may not work for your Medicare local carrier*

When to Order DXA Bone Density testing

Before transplantation:

Transplant candidates have higher risk of bone disease vs. general pop

DXA: lumbar spine, femoral neck, total hip, 33% radius

Trabecular Bone Score (if available with DXA software)

Calculate FRAX® Fracture risk prediction

Spine imaging: thoracic & lumbar spine, or vertebral fracture assessment (VFA) by DXA, look for occult vertebral fractures,

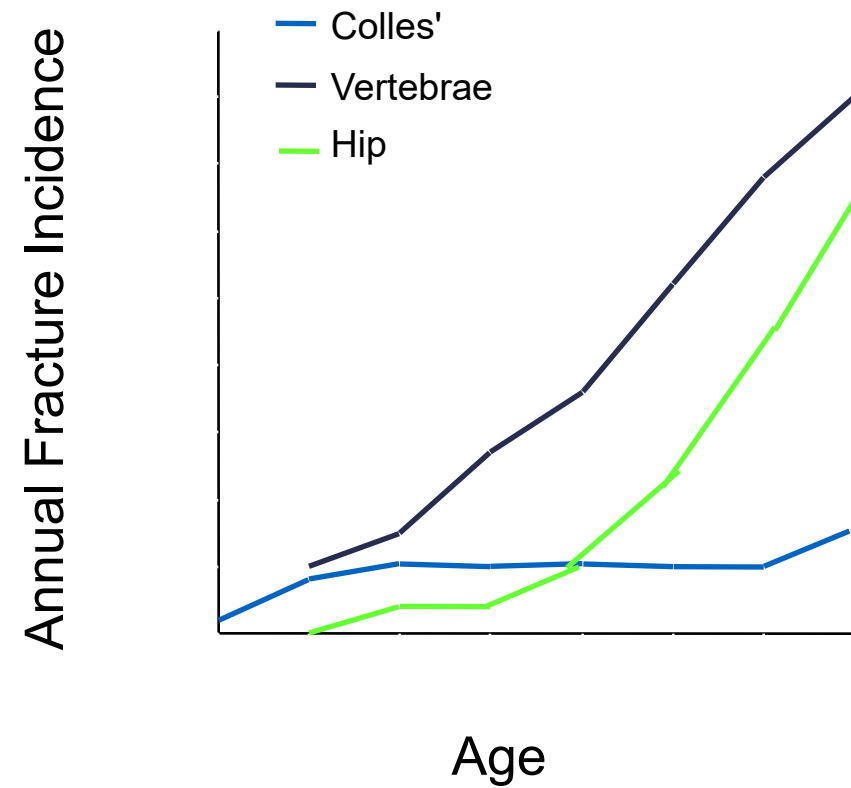
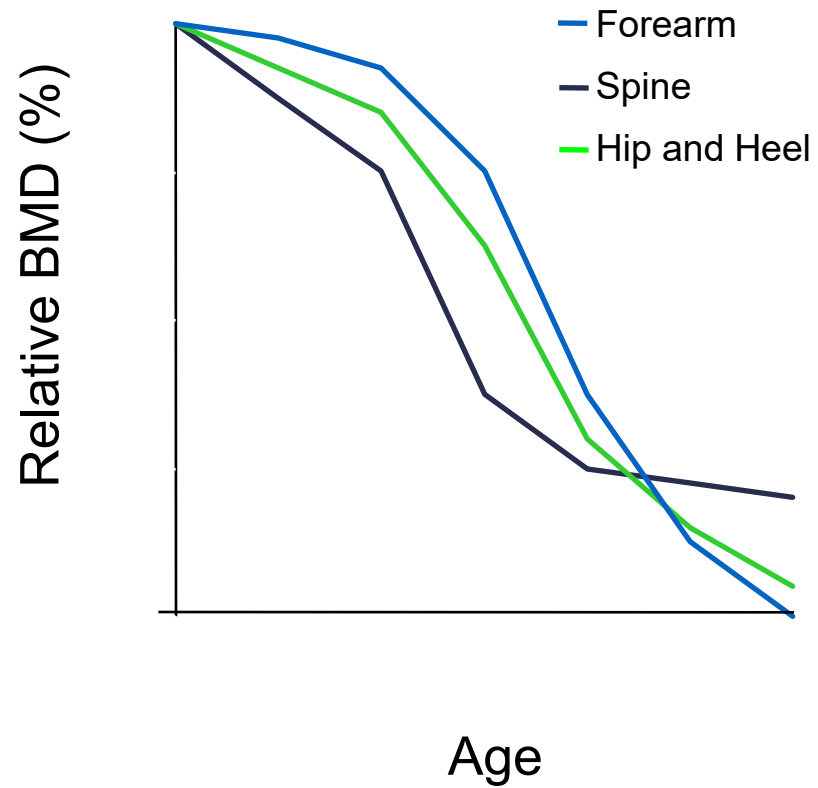
A normal DXA Bone Density does not protect against post transplant fractures

Fractures can occur even mildly low bone density

Repeat DXA yearly while on glucocorticoid treatment

As T-scores (BMD) Get Worse, Fracture Risk Increases

* Remember: Only ~1/3 of spine fractures are acutely painful



How Do You Interpret DXA Bone Density Results?

World Health Organization (WHO) DXA Classification

T-score *Postmenopausal women, men ≥ 50*

Normal ≥ -1

Osteopenia < -1 and > -2.5

Osteoporosis ≤ -2.5

Severe
Osteoporosis ≤ -2.5 with Fracture

When Should You Send a Patient for Imaging of the Spine?

Get a Lateral spine X-ray or VFA on a DXA or CT scan or MRI :

- When the patient has **Osteopenia** (T-score is < -1.0) and at least one :
- **Women age ≥ 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 ≥ 5 mg of prednisone or equivalent per day for ≥ 3 months**

ISCD Official Position

www.ISCD.org

ISCD offers a 1/2 day Vertebral Fracture
Recognition course

Fracture Risk Prediction Tool: FRAX®

The image shows a screenshot of the FRAX website. The top navigation bar includes links for Home, Online Calculation, FRAXplus®, Paper Charts, About, FAQ, and References, along with a MyFRAX® button. A language dropdown menu is set to English. The main content area features a 'Welcome FRAX® Fracture Risk Assessment Tool' message. A large green number '44381265' is displayed, representing the number of individuals with fracture risk assessed since 1st June 2011. Below this, a red 'Calculate now' button is visible. To the right, the 'Calculation Tool' section is shown, which includes a questionnaire with 12 items. Items 1 through 11 are listed on the left, and item 12, 'Femoral neck BMD', is on the right. A 'Calculate' button and a 'Clear' button are positioned below the questionnaire.

FRAX®

Home Online Calculation FRAXplus® Paper Charts About FAQ References MyFRAX®

English

Welcome
FRAX®
Fracture Risk Assessment Tool

44381265
Individuals with fracture risk
assessed since 1st June 2011

Calculate now

Calculation Tool

Please answer the questions below to calculate the ten-year probability of fracture with or without BMD.

Continent Select a continent Country US (Caucasian)

Local Reference Reference (optional)

About the risk factors ⓘ Individuals with fracture risk assessed since 1st June 2011 : 11,238,516

Questionnaire

1. Age (between 40 and 90 years) 71

2. Sex ☒ Female ☐ Male

3. Weight kg 0 kg/cm

4. Height cm 0

5. Previous Fracture ☒

6. Parent Fractured Hip ☒

7. Current smoking ☒

8. Glucocorticoids ☒

9. Rheumatoid arthritis ☒

10. Secondary osteoporosis ☒

11. Alcohol 3 or more units/day ☒

12. Femoral neck BMD GE-Lunar X g/cm²

Calculate Clear

2025 New website: <https://www.fraxplus.org/calculation-tool?country=9>

New Adjustments for FRAX®

- Recency of fracture
- Dose of steroids
- Trabecular bone score
- Duration of diabetes
- Recent falls
- Discordance: femoral neck vs. lumbar spine
- Hip axis length
- Hyperparathyroidism
- Number of prior fractures

Note: FRAX subscription fee \$50/year to use these features

Osteopenia and FRAXplus[®]

Age	53	Current smoking	No	with BMD	
Sex	Female	Glucocorticoids	Yes	T-score	-1.08
Weight	68.9 kg	Rheumatoid arthritis	No	BMI	23.8
Height	170.2 cm	Secondary osteoporosis	No		
Previous Fracture	Yes	Alcohol 3 or more units/day	No		
Parent Fractured Hip	No				

THE TEN-YEAR PROBABILITY OF FRACTURE

Major osteoporotic	15 %
Hip Fracture	1.0 %

PROBABILITY ADJUSTED ACCORDING TO RECENT FRACTURE

Previous Fracture	Vertebral
Time since previous fracture	1 to 6 months
Adjusted Major osteoporotic	15% → 35%
Adjusted Hip Fracture	1.0% → 1.9%

New FRAX[®] calculation

Test an alternative adjustment

Adjust your results with FRAXplus[®]

- Multiple additive adjustments are not possible as there is no evidence base available to inform on the accuracy of multiple adjustments.

When Should I Refer A Patient To An Osteoporosis Clinic?

When you do not feel comfortable treating with osteoporosis medications

When the patient has not tolerated OP meds

When a patient has already been taking an oral bisphosphonate for 3-5 years

When a patient has CKD 3b or worse

When a patient continues to have fractures

Unexplained or difficult to treat bone related labs

3 Reasons Patients Object to Taking Osteoporosis Medications

1. Cost
2. Fear of medication side effects
3. Lack of understanding about risks of osteoporosis and fractures

Often, they want someone to sit and review these details with them

“Don’t believe everything you read on the internet” - Abraham Lincoln

Pediatric Transplant Patients

Long term survival after transplant

6 X incidence of fracture compared to healthy population

High risk for vertebral fractures & scoliosis

Delayed growth and skeletal maturation

DXA hard to interpret: short stature, skeletal delay

DXA scores don't correlate well with fracture risk

Bone biopsies decreased bone turnover, high matrix mineralization.

Standard Lab Tests To Look For Secondary Causes of Bone Loss

Primary

1. CBC
2. Chemistry Profile
3. Phosphorus
4. Magnesium
5. PTH
6. TSH
7. 25-OH Vitamin D
8. 24 hr. urine calcium, creat.
9. Total testosterone_(men 50–69 years)

Note: ***Biotin may interfere with assays***

Further consideration:

SPIEP, free light chains, UPIEP

Celiac profile/IgA

Iron/Ferritin

Homocysteine

Prolactin

Urine /salivary cortisol, DST

Tryptase, urine methylhistamine

Bone Turnover Markers

(P1NP, C-telopeptide, BSAP)

Vitamin B6

3 Rare Bone Conditions Not to Miss

(treatable)

1. Hypophosphatemia- low serum phos, bone/muscle pain, fractures, high urine phos, elevated FGF -23 hormone: look for mesenchymal tumor, resect for cure
2. Hypophosphatasia-low serum alkaline phosphatase (≤ 30), fractures, **elevated Vit B6**, abnml ALPL gene; treat with asphotase-alpha to stop fractures
3. Hypoparathyroidism- low serum calcium, low PTH level, treat with 1-84 PTH to stabilize

Non-Prescription Treatment for Bone Health and Fracture Prevention

1. Correct Vitamin D levels, 25-OH Vitamin D above 30ng/mL, with vitamin D3
2. Get adequate calcium through diet ~1,000mg daily, 600mg max per serving, use calcium citrate to “fill in gap”; verify with 24 hr urine, it does not help to take more calcium than needed.
Note: loop and thiazide diuretics, steroids can affect urine calcium
3. Exercise & Tai Chi: to provide a mechanical load to bone and for improved balance
4. Avoid cigarette smoking and heavy alcohol consumption

Osteoporosis Medications

- Goal: reduce risk of fracture
- Antiresorptive medications:
 - Bisphosphonates: *Beware Renal($eGFR \geq 35$) & GI (GERD, stricture)*
 - Oral: alendronate , residronate, ibandronate
 - IV : zoledronate (Reclast®) slow infusion
 - Denosumab (Prolia®) *subcutaneous every 6 months***
 - New in 2025 :Generics available
 - In CKD: Monitor for hypocalcemia weekly for the first month after Dmab administration and monthly thereafter
- Anabolic drugs: Ideally Use First
 - teriparatide (Forteo®), *self injection nightly, x 2yrs***
 - abaloparatide (Tymlos®), *self injection nightly, x 2 yrs***
 - romosuzumab (Evenity ®) *subcut, office, monthly x 1 yr***

Medication Side Effect Concerns

Rebound bone loss/vert fractures with denosumab stop

Transition with bisphosphonates & monitor

Osteonecrosis of Jaw: rare, post invasive dental work, use chlorhexidine mouth wash, abx (bisphosphonates & densoumab), f/u

Atypical femur fracture: rare, after 4-5 years treatment, "drug holiday", ask about thigh pain (Bisphos. & densoumab), x-ray femur if 3yrs on therapy

Osteosarcoma: (theoretical) PTH analogues & radiation

Hypercalcemia: anabolic medications

Hypocalcemia: denosumab, renal patients

MI & CVA: romosuzumab

Long term monitoring

Labs: Vit D, calcium, creatinine, BTMs

Annual DXA bone density (hips, spine, 33% radius)

Bone Turnover Markers (PINP, Bone Spec. Alk Phos, C-Telopeptide)

Spine X-rays/MRI if height loss, back pain

Femur imaging if thigh pain or >3 yrs on bisphosphonates or denosumab
(ISCD guidelines)

Re-evaluate, maybe change medication if worse

Consider “drug holiday”(careful with denosumab)

Kidney Transplant Patients

Bone loss: greatest in 1st 6-18 months post txp, 4-9%

Assoc. with low estradiol & testost., age, GCS, rxn, PTH, loop diuretics, opiates

IV Zoledronic acid prior to kidney tplant attenuated bone loss in forearm vs.placebo

Fractures: risk factors: previous fracture, age, diabetics,

locations: hips, long bones, feet vs. spine & ribs

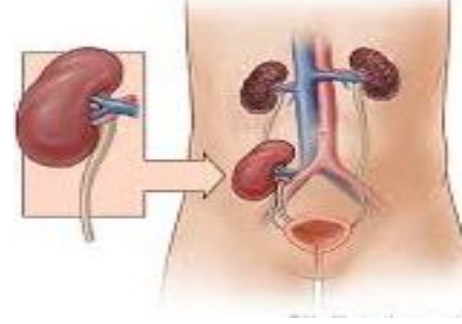
Post transplant: 34% increase in hip fractures compared to continued dialysis pts.

Treatment concerns: Bisphosphonates & possible renal toxicity, give slowly

Teriparatide/abaloparatide & hyperparathyroidism

Denosumab & hypocalcemia

Labelled bone biopsy sometimes required in renal transplant patients to evaluate for adynamic bone prior to bisphosphonate therapy



Kidney/Pancreas Transplant Case

64 yo female, school administrator

Age 50 **kidney and pancreas transplant**, steroids per protocol.

Fracture history & DXA:

Age 51-64: **distal radius fx**, femoral condyle fx, **prox humerus fx, wrist fx**

Age 51 DXA, lumbar spine L1-L2 1.0, femoral neck -1.9, total hip -1.4.

Age 64 DXA, lumbar spine L1-L2 -0.3, **femoral neck -2.9, total hip -2.7**

Nutrition & labs:

Age 56 VEGAN.

Age 58 Vitamin D deficiency, level was 24, age 60 was 23, at 64 is 19

Parathyroid hormone elevated at 177

Other risk factors: Age 15 Type 1 diabetes, resolved after transplant.

Severe HAs, sees Neuro, punctate lesions on MRI

Kidney/Pancreas T'plant Case

Next?

Labs?

Treatment?

non-prescription

Rx

Next DXA ?

Other monitoring?

Liver Transplant Patients



Bone loss:

3.5-24% in first year

Risk factors: Cholestatic liver disease

Previous fracture

High MELD scores

Low BMI

Post menopausal

Older age

Fractures:

24-65%

Ribs and spine most common

Highest in 1st 6-12 months

Risk factors: Prior fracture, Prednisone dose, Women with PBC

Treatment issues: Liver activates vitamin D to 25-OH Vitamin D

Bisphosphonates: case by case basis

Anabolic therapy may be appropriate if low turnover

Crawford BAL et al *Ann Intern Med.* 2006;144:239-248

Abate et al *Endocrine Practice* 27 (2021) 426-432

Yadav et al *Nutr Clin Pract* 2013 28: 52

Dove L et al. AASLD AST Practice Guideline on adult liver transplantation. *Hepatology.* 2026;83:1609–1645

Liver Transplant Case

61 yo female, retired

Age 60 liver transplant for alcoholic cirrhosis, steroids per protocol

Fracture history: age 60 fall, left tibia fracture, healed with boot.

DXA

Age 60 (pre-tplant) **DXA**, lumbar spine -1.6, femoral neck -1.1, total hip -0.3, RX alendronate, GI upset

Age 61 post tplant **DXA** Lumbar spine L1-L2 -1.4, femoral neck -1.6 (0.815), total hip -0.8

FRAX: 22% MOF, 2.6% hip fracture risk. BHOOF guidelines she would benefit from receiving treatment to reduce her risk of fracture.

Labs: post tplant

24-hour urine calcium, normal at 126 mg.

Vitamin D is 35

Hypomagnesemia, level was 1.5. now on MG supplement

CKD 3b, eGFR 39

Liver Transplant Case (cont'd)

Next?

Labs?

Treatment?

non-prescription

Rx

Next DXA?

Other monitoring?



Heart Transplant Patients

Bone loss: 3-11% in first year

Fractures: 14-36% in first year,
22-35% long term
fractures occur at osteopenic T-scores (-1.5)

Treatment issues: 92% vitamin D deficient
20% CKD III

ISHLT Heart Transplant Guidelines 2010



Pre-transplant

- Screen & treat all candidates
- Spine x-ray adults to screen for vert. fractures
- Target Vit D level 30ng/mL
- Baseline DXA for adults
- Rx Bisphosphonates for OP
- Calcium, physical activity

Note : Guidelines were pre denosumab, abaloparatide and trabecular bone score

Post Transplant

- Rx Bisphosphonates first year
 - **Activated vit D is not first line Rx**
 - **Don't use Calcitonin**
- DXA again a 1 year
- If ≥ -1.5 & no GCS: stop bisph.
- DXA again 2 yrs if osteopenia
- DXA again 3 yrs if nml
- Monitor for fractures

Case

69 yo w ♀

Age 26- TAH, BSO; Rx estrogens "few years"

Age 33- DXA Bone Density test= "low"

Failed treatments:

SQ calcitonin-GI

alendronate -GI

raloxifene–Hot flashes

Age 50: Ischemic heart dz

Age 55- DXA hip T-score= -3.5

Rx risedronate x 2yrs

Age 57: Cardiomyopathy

Heart T'plant list



Case (cont'd)



Age 59- cardiac transplant

prednisone 5mg/day

re-started risedronate = GI issues

switched to ibandronate

Age 64 DXA Femoral Neck T-score = -2.4

What would you do next?

Optimize vit D & calcium?

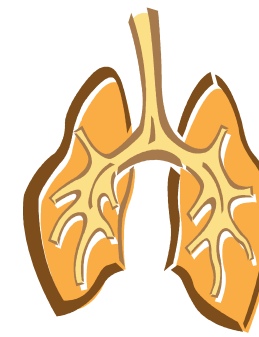
Stop ibandronate?

Switch to anabolic medication?

“Drug holiday” and monitor DXA?

Request bone health consult?

Lung Transplant Patients



Highest incidence of osteoporosis compared to other patients with solid organ transplant.

Bone loss: 2-5% in first year
37% osteoporosis at time of t'plant (previous steroids)

Fractures: 18-37% in first year
fractures occur at T-score of -1.5

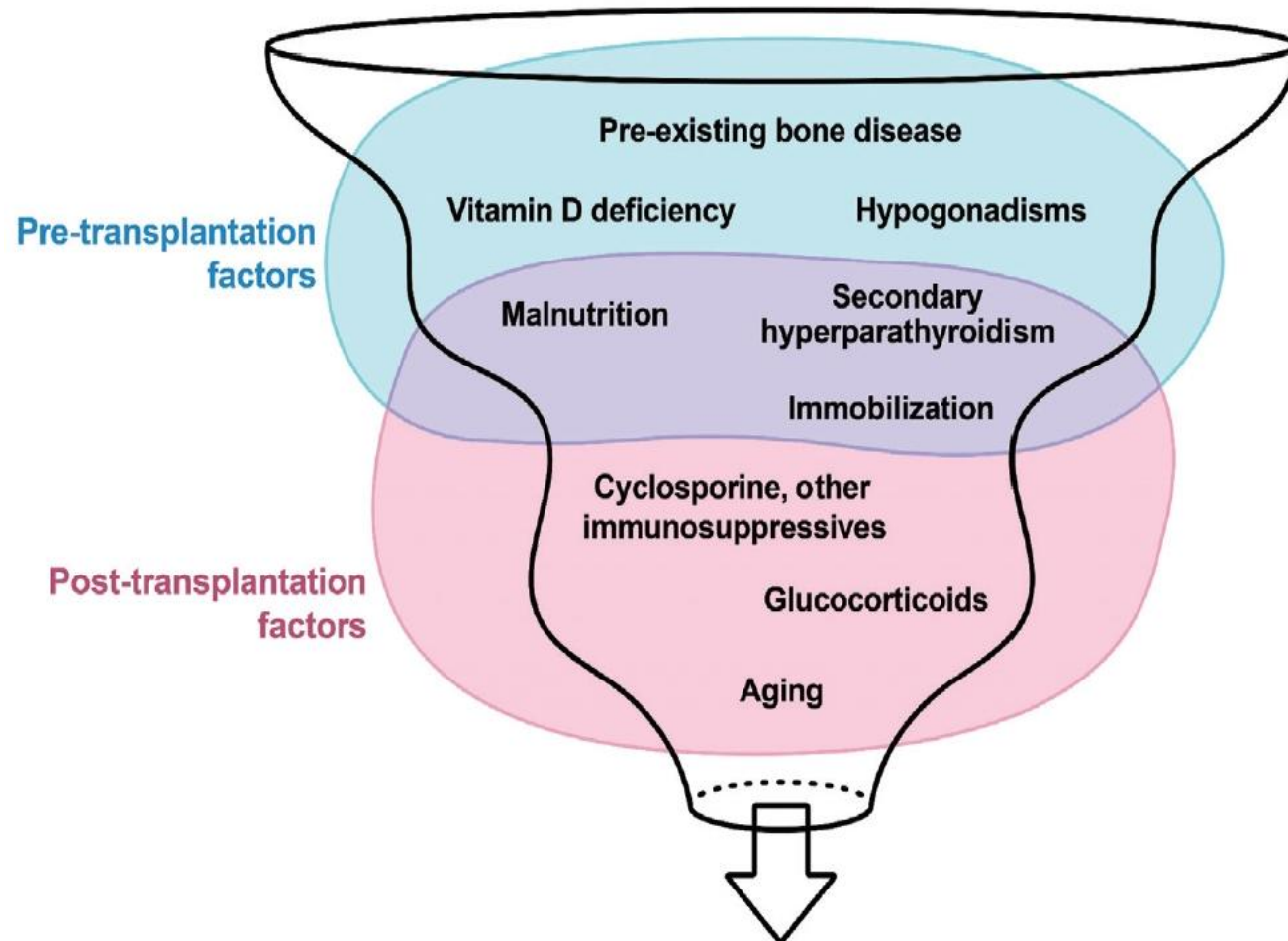
Treatment issues: often an opportunity to treat before t'plant
Teripartide treatment appears to be more successful than in kidney transplant.

Raven et al. *JCEM Case Reports*, 2024, **2**, 1–4 <https://doi.org/10.1210/jcemcr/luae026>

Shane et al. *Am J Med*. 1996 Sep;101(3):262-9.

Hariman et al. *Journal of Osteoporosis*. 2014, <http://dx.doi.org/10.1155/2014/573041>

Funnel Effect on Bone Health in the Transplant Population



Take Home Points:

Fractures affect morbidity & mortality

Transplants increase fracture risk

Evaluate bone health pre-transplant and treat

DXA, Labs, nutrition, exercise, fall prevention

A normal DXA Bone Density does not protect against post transplant fractures

Height loss may be the only sign of a compression fracture

Anabolic meds work best if used first

All medications require monitoring and are not used forever

Resources:

www.bonehealthandosteoporosis.org Bone Health and Osteoporosis Foundation

www.ISCD.org Internat. Soc. Clinical Densitometry

www.IOF.org Internat. Osteoporosis Foundation

Bone Health & Solid Organ Transplantation: 2019 ECTS Recommendations
Anastasilakis A D et al. Bone 2019 Oct;127:401-418

October 20th is World Osteoporosis Day!

Questions for us?

Thank you