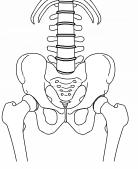


Update: Osteoporosis & The Solid Organ Transplant Patient











Bobo Tanner MD
Anna Richmond NP
Vanderbilt Osteoporosis Clinic
Division of Rheumatology
Oct 13,2025

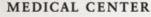


BT Disclosures

Research:

Research Support: Amgen

Advisory Panel: Kyowa Kirin



2024 Organ Transplants in US:

48,150 transplants, deceased & living donors

Kidney: 27,760

Liver :11,458

Heart: 4,572

• Lung: 3,340

Pancreas w/w-out kidney: 847

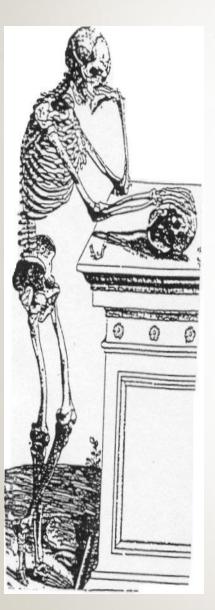
76-97% survival in last 15 years

107,689 on the wait list, mostly kidney





Agenda



Why are you thinking about bone?

- Osteoporosis overview
- DXA Bone density testing
- Labs
- Medications & Management
- Cases & Organ Specific issues
- Take home points



Defining Osteoporosis:

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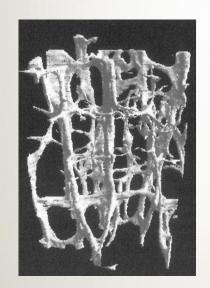


Normal Bone

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



Hip fracture, w/wout DXA
Clinical vertebral, proximal humerus or pelvis fx with osteopenia



Osteoporotic Bone

¹Consensus Development Conference: Diagnosis, Prophylaxis, and Treatment of Osteoporosis. *Am J Med* 1991;90:107-110 ² Kanis JBMR 1994



Hip Fracture:

Devastating Event

Mortality rate same as breast cancer

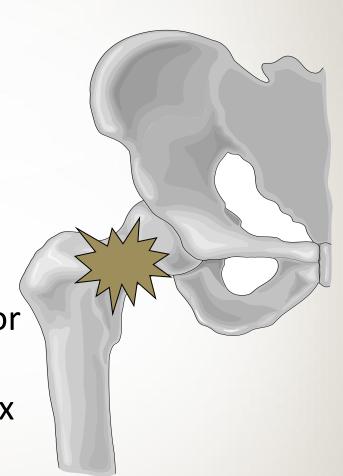
20% excess mortality in the first year

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





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Hip Fracture: Devastating Toll: "The 4 Ds"

1. Death^{2,6}
Mortality rate same as breast cancer

2. Disability^{1,2}
50% incapacitation

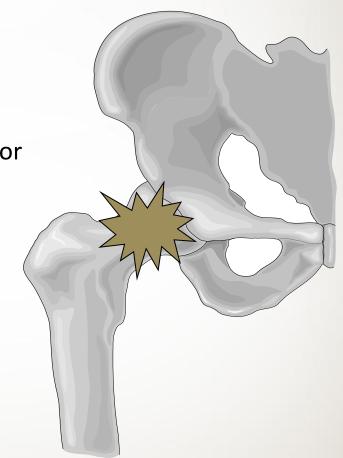
3. Dependence^{1,2}
20% of females need assisted living or nursing home

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





Osteoporosis & Fracture

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After Transplant

Orgar

Osteoporosis Prevalence

Fracture Prevalence or Rate



Lumbar spine 17%-49% Femoral Neck 11%-56%

50% overall

73% overall

Kidney

Radius 22%-52%

Kim JK etal. Endocrinol Metab 2024;39:267-282

https://doi.org/10.3803/EnM.2024.

Liver

46% overall

Lumbar spine 2%-24%

Heart

Vertebral 33%-36%

prevalence

18%-37% rate

24%-65% rate

7%-44% prevalence

Lumbar spine 4%-10% Femoral neck 5%-8%

Lumbar spine 6%-10% Femoral neck 6%-11%

Lumbar spine &

Femoral neck 2%-5%



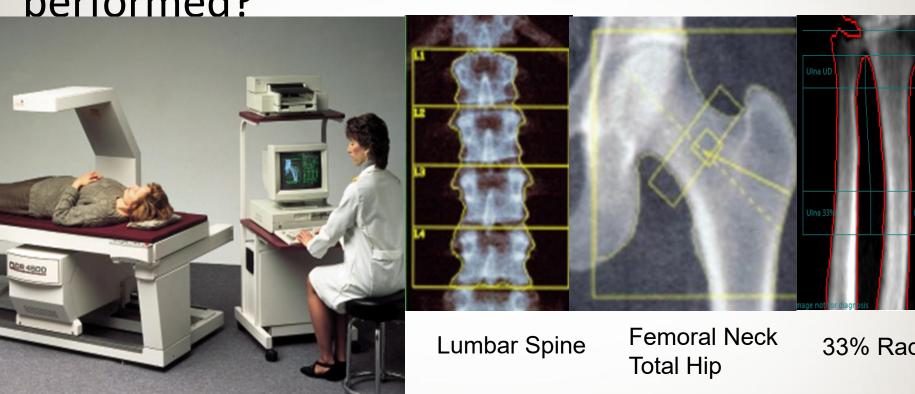
Specific
Organ
Transplant
&
Localizatio
n of
fractures

Common after lung, cardiac and liver transplantations Common after kidney transplantation

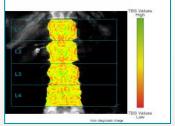


When should DXA Bone Density testing be

performed?



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

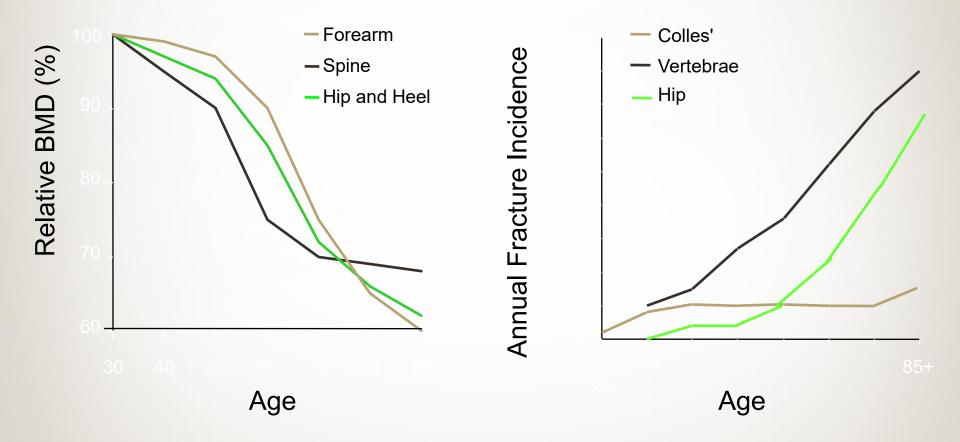
Before transplantation:

- Transplant candidates have higher risk of bone disease vs. general pop
- Evaluate and manage bone health before the transplantation
- 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





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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

 \leq -2.5

Severe Osteoporosis

 \leq -2.5 with Fracture



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

- Get <u>a Lateral spine X-ray</u> 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 ≥ 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

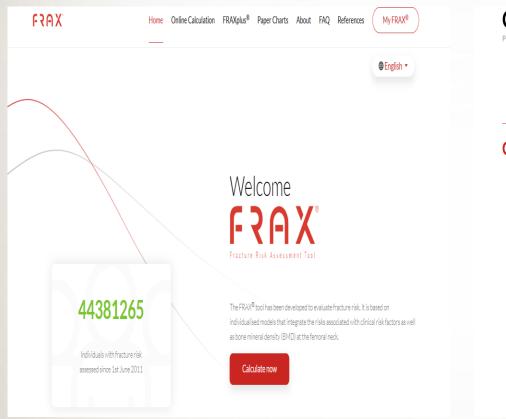
ISCD Official Position

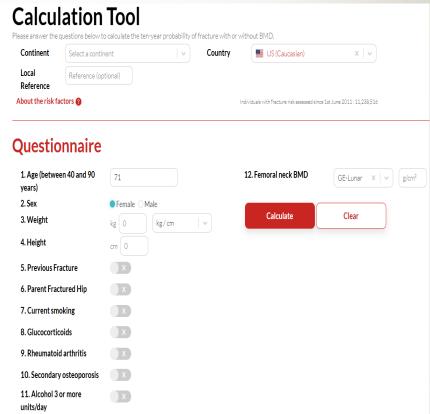
www.ISCD.org

ISCD offers a 1/2 day Vertebral Fracture Recognition course



Fracture Risk Prediction Tool: FRAX®





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



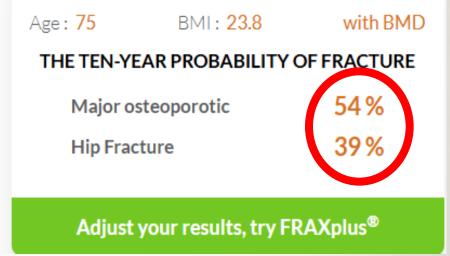
Osteopenia & Fracture Risk (FRAX®)

Two women with the same femoral neck <u>T-score of -2.3</u> *Osteopenia*

55 yo white female, BMI of 24 No additional clinical risk factors



75 yo white female, BMI of 24
Maternal history of hip fracture
Prior humerus Fx, chronic prednisone use



Despite the same diagnosis, their fracture risk is markedly different



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)

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

Note: Biotin may interfere with assays



3 Rare Bone Conditions Not to Miss

(treatable)

- 1. Hypophosphatemia- low <u>serum phos</u>, bone/muscle pain, fractures, high urine phos, elevated FGF -23 hormone: look for mesenchymal tumor, resect for cure
- 2. Hypophosphatasia-low <u>serum alkaline</u> <u>phosphatase(<30)</u>, fractures, <u>elevated Vit B6</u>, 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 > 35) & GI (GERD, stricture)
 - Oral: alendronate, residronate, ibandronate
 - IV : zoledronate (Reclast®) slow infusion
 - Denosumab (Prolia®) subcut. 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: <u>Ideally Use First</u>
 - 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 Dmab stop
 - Transition with bisphos & 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



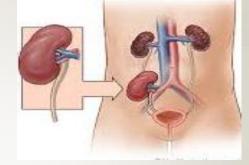
Long term monitoring

- 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 bisphos or dmab (ISCD guidelines)
- Re-evaluate, maybe change medication if worse
- Consider "drug holiday" (careful with denosumab)



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Kidney Transplant Patients



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

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

IV Zol 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 T'plant 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



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 have been used in PBC

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



Liver Transplant Case

61 yo female, retired

Age 60 liver transplant for alcoholic cirrhosis, steroids per protocol <u>Fracture history:</u> 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. BHOF 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

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 早
- 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

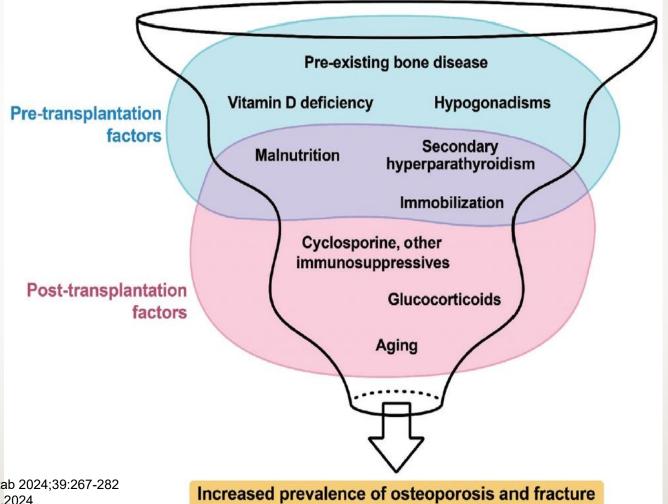
fractures occur at T-score of -1.5

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

Raven at 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





Bone Health & Solid Organ Transplantation:

2019 ECTS Recommendations

- Glucocorticoids(GCs): use lowest dose possible for graft survival
- Tacrolimus may limit GCs use;more modest BMD reduction than cyclosporine
- Sirolimus & everolimus (mTOR inhibitors), reduce bone turnover, mostly decreased resorption & reduce GCs use, good for bone?
- Other meds, MMF, may reduce use of GCs, therefore good for bone?



Bone & Solid Organ Transplantation:

2019 ECTS Recommendations (cont'd)

- Kidney: KDIGO CKD-MBD 2017 guidelines:
 - first 12 months p tplant, eGFR > 30 ml/min, low BMD:
 - Consider vitamin D, calcitriol/alfacalcidol, and/or antiresorptive agents, possible labelled bone bx
 - After that year, what next?
- **Liver:** pre-tplant DXA, spine x-ray, again 3-6 mos p tplant, may require more Vit D, start BPs early p tplant, DMAB if renal insuff or can't take BPs, Dmab well-tolerated ,increased BMD p tplant liver, kidney, pancreas
- **Heart:** Pre-plant labs, DXA spine x-ray, correct Mg; Rx BPs p tplant
- Lung: Pre-tplant DXA, spine imaging, Vit D, BPs



NP Perspective



Pediatric Transplant Patients

- Long term survival after t'plant
- 6 X incidence of fx compared to healthy pop.
- 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.



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

[&]quot;Don't believe everything you read on the internet" - Abraham Lincoln



"I don't want all my teeth to fall out"

- American Association of Oral and Maxillofacial Surgeons' Position Paper on Medication-Related Osteonecrosis of the Jaws - 2022 Update
- Osteonecrosis of the jaw: Exposed bone or bone that can be probed through an intraoral or extraoral fistula(e) in the maxillofacial region that has persisted for more than 8 weeks.
- Rates of ONJ
 - Placebo 0-0.02%
 - IV Reclast (zoledronic acid) ≤0.02% (≤ 2 per 10,000)
 - oral bisphosphonates ≤0.05% (≤ 5 per 10,000)
 - denosumab 0.04% to 0.3%
 - romosozumab 0.03% 0.05%
- the risk of MRONJ among osteoporotic patients exposed to BPs following tooth extraction range from 0 to 0.15 %
- For osteoporotic patients exposed to DMB, the risk for MRONJ following tooth extraction was
 1 %



"I heard once you start taking those bone medications you can't stop"

- Rebound bone loss after stopping Prolia (denosumab) is a real concern and thus requires an exit strategy when discontinuing therapy
 - FREEDOM extension trial showed 10 years of denosumab therapy to be safe and effective
- Drug holidays really refers to bisphosphonate therapy
- Treatment of osteoporosis is different for each patient, it is possible to be off therapy for years and then re-institute therapy if worsening bone density, increased risk for fracture or if a fracture occurs



"bisphosphonates are first line"

 In patients who are at very high risk for fracture such as those with recent fractures and/or very low BMD (T score < -3.0) anabolic therapy with Forteo (teriparatide), Tymlos (abaloparatide), or Evenity (romosozumab) may be more appropriate/effective than treatment with bisphosphonate



Benefits of osteoporosis treatment

- Prevention of fractures
- Promotion of independence, quality of life



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



Questions for us?

Resources:

- www.bonehealthandosteoporosis.org Bone Health and Osteoporosis Foundation
- www.ISCD.org Internat. Soc. Clinical Densitometry
- www.IOF.org Internat. Osteoporosis Foundation

Thank you for concern about your patient's bone health!

October 20th is World Osteoporosis Day!