



Bone Health after Transplant

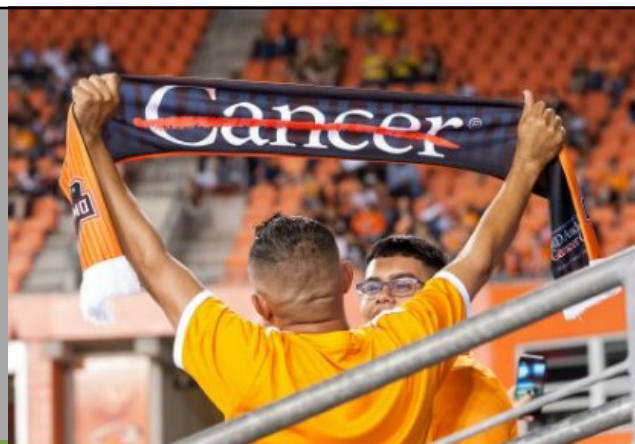
Celebrating a Second Chance at Life
Survivorship Symposium

April 30 - May 6, 2022



Huifang Lu MD, PhD
The University of Texas
MD Anderson Cancer Center

THE UNIVERSITY OF TEXAS
**MD Anderson
Cancer Center**
Making Cancer History®



Bone Health after Transplant

Huifang Linda Lu, MD PhD

Learning Objectives

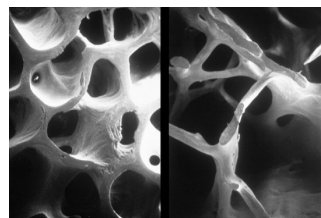
- Bone loss is common after transplant
- Bone loss can cause fractures in men and women survivors
- There are many risk factors that lead to fractures
- Lifestyle change is the cornerstone of bone health
- There are medications to treat osteoporosis and prevent fracture safely and effectively

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Why is bone health important?

- Bone loss causes healthy bone to be “porous” as osteoporotic
- Osteoporotic bone is more fragile with increased risk of fractures
- Osteoporosis is known as a silent disease; it can progress undetected for many years without symptoms until a fracture occurs.
- Spine fractures can cause severe back pain, loss in height, loss of lung function and change in one’s posture
- Fracture can cause inability for self care, or prolonged disability



Normal bone

Osteoporotic bone



Compression fracture:
Lumbar spine

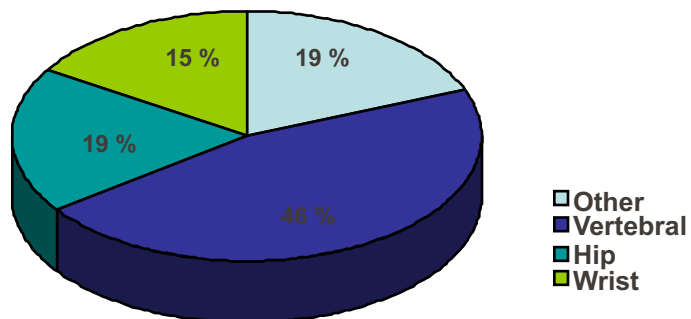
ACR Image Library

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Osteoporosis affects the **entire** skeleton

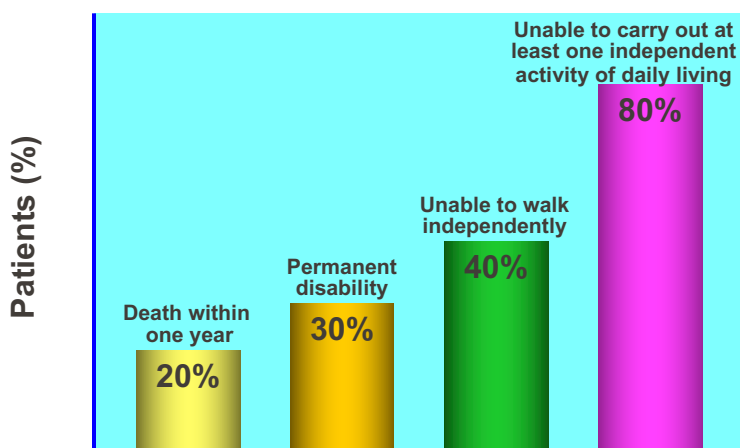
- Osteoporosis is responsible for near 2 million vertebral and non-vertebral fractures annually
- Spine, hip, and wrist fractures are most common



NIH/ORBD (www.osteoporosis.org), 2020

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One year after hip fracture



Cooper C, Am J Med, 1997;103(2A):12S-17S

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Osteoporosis Prevalence

Affects 200 million women worldwide¹

- 1/3 of women aged 60 to 70
- 2/3 of women aged 80 or older

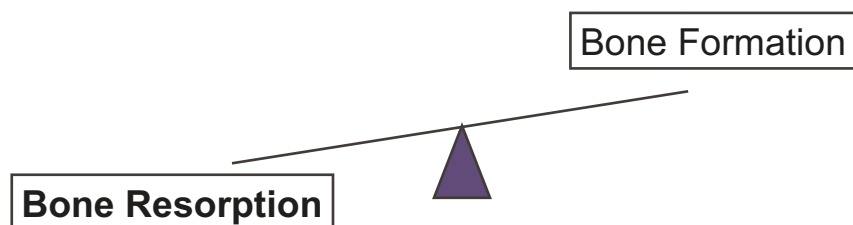
Approximately 30% of women over the age of 50 have one or more vertebral fractures²

Approximately one in five men over the age of 50 will have an osteoporosis-related fracture in their remaining lifetime¹

1. IOF, 2005 (www.osteofound.org)
2. Dennison E & Cooper C, Horm Res. 2000;54 suppl 1:58-63

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Bone Loss



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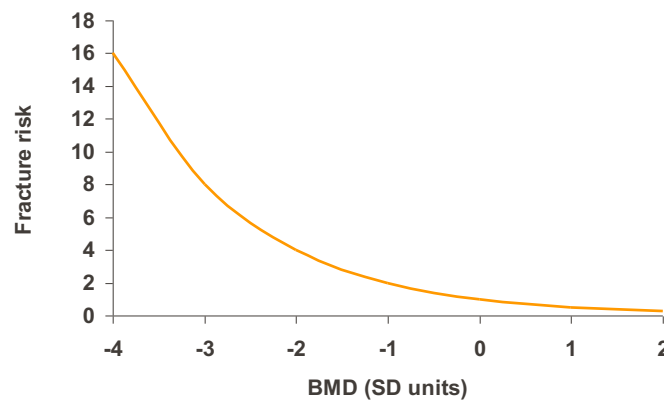
General risks for osteoporosis and fractures

- Older age
- Female gender
- Previous low impact fracture
- Family history of hip fracture
- Glucocorticoid therapies
- Current tobacco use
- High daily alcohol intake (≥ 3 units/day)
- Low body weight
- Other secondary causes of osteoporosis

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Relationship between bone mineral density and fracture risk



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Measuring Bone Mineral Density

Dual-energy x-ray absorptiometry (DXA):

- Provides a 2-D measure of bone mineral density
- Office based
- Central DEXA
 - **Gold standard**
 - Measures spine, hip, or total body BMD



Peripheral DEXA

- Measures wrist, heel, or finger BMD

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Who should get a bone density study?

- Women aged 65 and older and men aged 70 and older
- Postmenopausal women younger than 65 and men ages 50-69 in the presence of clinical risk factors:
 - Low body weight
 - High risk medication (such as glucocorticoid)
 - Low impact fracture
 - With a disease or its treatment associated with bone loss

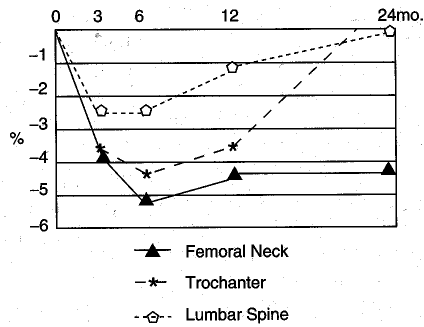
International Society for Clinical Densitometry 2007
National Osteoporosis Foundation 2008

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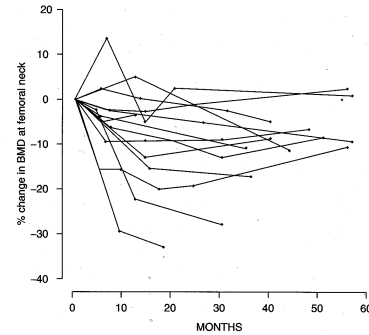
Rapid bone loss occurs soon after the transplant

Bone loss after self transplant



2003 Br J Haematol. 121(3):462-468

Bone loss after donor transplant



1999 JBMR 14:342-350

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Why bone loss happens in people who received a transplant?

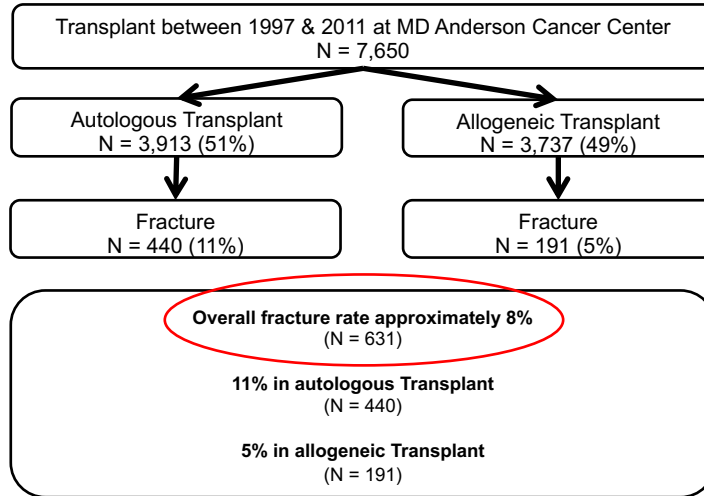
- Underlying disease and its treatment
- Low sex hormones
 - Premature menopause in women
 - Low testosterone in men
- Chemotherapy
- Radiation
- Graft versus host disease treatment (glucocorticoid)
- Vitamin D deficiency
- Malabsorption

Eberling JBMR 1999
Weilbaecher Biol BMT 2000

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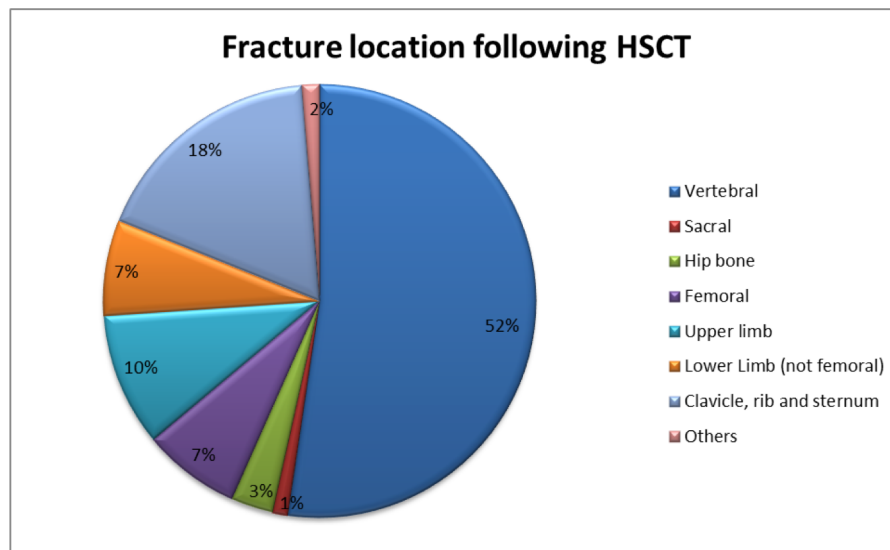
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Fracture occurs in patients received transplant



Pundole and Lu 2015 JCO
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Fracture location following stem cell transplant



Pundole and Lu 2015 JCO

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Characteristics of transplant patients who fractured (N=631)

Mean age	49.29 (± 13.51) years
Male	55%
Hematologic malignancy	89.5%
Mean time to fracture	33 (± 10.45) months
Male vs. female	similar rate
Vertebral fracture	M:F 56%:53%
By year 5	fracture seen in 12%
By year 15	fracture seen in 23%

Pundole and Lu 2015 JCO

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Fracture Risk Assessment - FRAX – predict the 10-year risk of fracture in transplant patients

The screenshot shows the FRAX WHO Fracture Risk Assessment Tool interface. The questionnaire includes the following information:

- Country: US (Caucasian)
- Age: 41
- Sex: Male
- Weight (kg): 68.4
- Height (cm): 162
- Previous Fracture: No
- Parent Fractured Hip: No
- Current Smoking: No
- Glucocorticoids: No
- Rheumatoid arthritis: No
- Secondary osteoporosis: No
- Alcohol 3 or more units/day: No
- Femoral neck BMD (g/cm²): 0.718

The results displayed are:

- BMI: 26.1
- The 10-year probability of fracture (%):
- without BMD
- Major osteoporotic: 1.7
- Hip Fracture: 0.1

Conversion tools are shown for Weight (Pounds to kg) and Height (Inches to cm).

Treatment recommended for:

Major osteoporotic risk: > 20%

Hip fracture risk: > 3%

Pundole and Lu. Arch Osteoporosis 2018

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When to check on bone health after transplant

- **Risk factor screening**
 - Lifestyle issues (tobacco use, excessive alcohol, sedative)
 - Fragility, fall and fracture risk
 - Medications
- **Bone density scan (DXA) and/or fracture risk assessment (FRAX)**
 - 3 months post transplant, if not done before
 - At 3 months, if prolonged high-dose glucocorticoid was given
 - Follow up DXA at 12 months on treatment and every 1-2 years thereafter

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Bar 2020 Practice Guideline BBMT 10:1784

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How to improve bone health after transplant

- Take calcium daily
- Get enough vitamin D
- Start weight-bearing exercises
- Reduce fall risk
- Keep a healthy weight
- Limit alcohol intake
- Do not smoke

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What dietary and lifestyle modifications can I do?

- **Calcium:**
 - 1000 to 1200 mg/day in 2-3 divided doses from food or supplement
- **Vitamin D:**
 - ≥ 1000 IU/day to keep serum 25-hydroxy vitamin D levels 30 to 50 ng/mL (have your doctor check your levels periodically)
 - Vit D can be taken once daily or once per week
- **Personalized exercise:** at least 30 minutes per day
 - Weight-bearing impact exercise (eg, walking, jumping, skipping, bench stepping)
 - Resistance exercise (eg, weightlifting, resistance band exercise, pushups)
 - improve agility, strength, posture, and balance
 - may reduce the risk of falls
 - modestly increase BMD

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More on calcium

- **Calcium:**
 - 1000 to 1200 mg/day in 2-3 divided doses
- From Food
 - Milk or other dairy product
 - Seafood
 - Produce
- From Supplements
 - No more than 500 - 600 mg at a time

Food	Portion Size	Calcium
milk	8 oz	300 mg
yogurt	6 oz	310 mg
Mozzarella, part-skim	1 oz	210 mg
Sardines, canned with bones	3 oz	325 mg
Salmon, canned with bones	3 oz	180 mg
Shrimp, canned	3 oz	125 mg
Collard greens, cooked	1 cup	266 mg
Kale, cooked	1 cup	179 mg
Bok choy, cooked	1 cup	160 mg
Broccoli, fresh, cooked	1 cup	60 mg

Bonehealthandosteoporosis.org

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When do I need medications to treat osteoporosis?

- Fragility fracture
- Osteoporosis diagnosed by a DXA scan
 - Postmenopausal women
 - Men over age 50
- FRAX score estimated 10-year fracture risk
 - Major osteoporotic fracture risk > 20%
 - Hip fracture risk > 3%

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When do I need medications to treat osteoporosis?

When on prolonged treatment of **glucocorticoid** (for graft versus host disease)

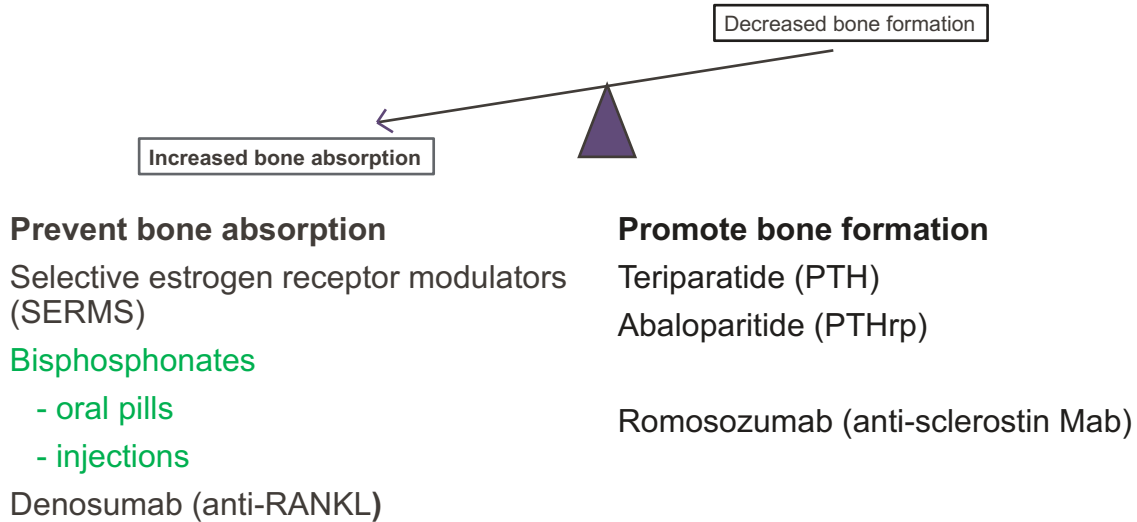
- Age > 40
 - Fragility fracture
 - Osteoporosis diagnosed by a DXA scan
 - Postmenopausal women
 - Men over age 50
 - FRAX score estimated 10-year fracture risk
 - Major osteoporotic fracture risk > 10%
 - Hip fracture risk > 1 %
- Age < 40
 - Fragility fracture
 - Severe osteoporosis or rapid bone loss

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Medications to treat osteoporosis



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Medications used to treat osteoporosis in transplant recipients

Drug	How to take	Efficacy	Adverse effect/concerns
Oral bisphosphonates <ul style="list-style-type: none"> Alendronate (Fosamax)¹ Risedronate (Actonel)¹ Ibandronate (Boniva)² 	1. Once every week 2. Once every month	+ / ++	<ul style="list-style-type: none"> Heart burn Caution with use in patient with abnormal kidney functions Lack of efficacy in preventing hip fractures by ibandronate
IV bisphosphonate <ul style="list-style-type: none"> Zoledronic acid (Reclast) 	Infusion by the vein once a year	+++	<ul style="list-style-type: none"> Body ache and flu-like symptoms can occur, but self-limited Caution with use in patient with abnormal kidney functions
Anti-RANKL monoclonal antibody <ul style="list-style-type: none"> Denosumab (Prolia) 	Injection under the skin once every 6 months	Case report only	<ul style="list-style-type: none"> Clinical trial is ongoing Rebound bone loss and fracture can occur after stopping the medication Needs to be followed by bisphosphonate therapy

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Commonly heard concerns:

- *“I read terrible things about these medications.”*
- *“I have friends who took these medications and suffered unwanted side effects.”*

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How do we decide?

- The benefit of fracture prevention out-weighs the small risk
- Severe side effect such as the osteonecrosis of the jaw is very rare and often preventable
 - Regular dental cleanings at least every 6 months
 - Daily brushing and flossing
 - Check with your dentist before starting the medication
 - Drug holidays

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Take-home messages

- Bone health is important after transplant
- Bone loss can cause fractures in men and women survivors, leading to disability
- There are many risk factors contributing to fractures
- Lifestyle change is the cornerstone of bone health
- There are medications to treat osteoporosis and prevent fracture safely and effectively

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BLOOD & MARROW TRANSPLANT INFORMATION NETWORK
SURVIVORSHIP SYMPOSIUM

Questions?



Huifang Lu MD, PhD

Celebrating a Second Chance at Life Survivorship Symposium 2022

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