Bone Health after Transplant

Celebrating a Second Chance at Life Survivorship Symposium

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The University of Texas MD Anderson Cancer Center

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

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
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

![Pie chart showing fracture types](NIH/ORBD (www.osteo.org), 2020)

One year after hip fracture

- Unable to walk independently: 40%
- Permanent disability: 30%
- Unable to carry out at least one independent activity of daily living: 80%
- Death within one year: 20%

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

Affects 200 million women worldwide\(^1\)
- 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 fractures\(^2\)

Approximately one in five men over the age of 50 will have an osteoporosis-related fracture in their remaining lifetime\(^1\)

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

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Bone Loss

![Bone Loss Diagram](image_url)
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

Relationship between bone mineral density and fracture risk
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

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
Rapid bone loss occurs soon after the transplant

Bone loss after self transplant

Bone loss after donor transplant

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
Fracture occurs in patients received transplant

Transplant between 1997 & 2011 at MD Anderson Cancer Center
N = 7,650

- Autologous Transplant
  N = 3,913 (51%)
  Fracture
  N = 440 (11%)

- Allogeneic Transplant
  N = 3,737 (49%)
  Fracture
  N = 191 (5%)

Overall fracture rate approximately 8%
(N = 631)

11% in autologous Transplant
(N = 440)

5% in allogeneic Transplant
(N = 191)

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Fracture location following stem cell transplant

Fracture location following HSCT

- Vertebral: 52%
- Sacral: 18%
- Hip bone: 10%
- Femoral: 7%
- Upper limb: 7%
- Lower Limb (not femoral): 3%
- Clavicle, rib and sternum: 3%
- Others: 3%

Pundole and Lu 2015 JCO
MD ANDERSON CANCER CENTER
Characteristics of transplant patients who fractured (N=631)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>49.29 (± 13.51) years</td>
</tr>
<tr>
<td>Male</td>
<td>55%</td>
</tr>
<tr>
<td>Hematologic malignancy</td>
<td>89.5%</td>
</tr>
<tr>
<td>Mean time to fracture</td>
<td>33 (± 10.45) months</td>
</tr>
<tr>
<td>Male vs. female</td>
<td>similar rate</td>
</tr>
<tr>
<td>Vertebral fracture</td>
<td>M:F 56%:53%</td>
</tr>
<tr>
<td>By year 5</td>
<td>fracture seen in 12%</td>
</tr>
<tr>
<td>By year 15</td>
<td>fracture seen in 23%</td>
</tr>
</tbody>
</table>

Pundole and Lu 2015 JCO

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

Treatment recommended for:
- Major osteoporotic risk: > 20%
- Hip fracture risk: > 3%

Pundole and Lu. Arch Osteoporosis 2018

Huifang Lu MD, PhD
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

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
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

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

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

Bonehealthandosteoporosis.org
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%

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
Medications to treat osteoporosis

**Prevent bone absorption**
- Selective estrogen receptor modulators (SERMS)
  - Bisphosphonates
    - oral pills
    - injections
  - Denosumab (anti-RANKL)

**Promote bone formation**
- Teriparatide (PTH)
- Abaloparitide (PTHrp)
- Romosozumab (anti-sclerostin Mab)

**Increased bone absorption**
- Decreased bone formation

### Medications used to treat osteoporosis in transplant recipients

<table>
<thead>
<tr>
<th>Drug</th>
<th>How to take</th>
<th>Efficacy</th>
<th>Adverse effect/concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral bisphosphonates</strong></td>
<td></td>
<td>++/++</td>
<td>• Heart burn</td>
</tr>
<tr>
<td>• Alendronate (Fosamax)</td>
<td>1. Once every week 2. Once every month</td>
<td></td>
<td>• Caution with use in patient with abnormal kidney functions</td>
</tr>
<tr>
<td>• Risedronate (Actonel)</td>
<td></td>
<td></td>
<td>• Lack of efficacy in preventing hip fractures by ibandronate</td>
</tr>
<tr>
<td>• Ibandronate (Boniva)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>IV bisphosphonate</strong></td>
<td>Infusion by the vein once a year</td>
<td>+++</td>
<td>• Body ache and flu-like symptoms can occur, but self-limited</td>
</tr>
<tr>
<td>• Zoledronic acid (Reclast)</td>
<td></td>
<td></td>
<td>• Caution with use in patient with abnormal kidney functions</td>
</tr>
<tr>
<td><strong>Anti-RANKL monoclonal antibody</strong></td>
<td>Injection under the skin once every 6 months</td>
<td>Case report only</td>
<td>• Clinical trial is ongoing</td>
</tr>
<tr>
<td>• Denosumab (Prolia)</td>
<td></td>
<td></td>
<td>• Rebound bone loss and fracture can occur after stopping the medication</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Needs to be followed by bisphosphonate therapy</td>
</tr>
</tbody>
</table>
Commonly heard concerns:

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

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
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

Questions?

Huifang Lu MD, PhD
Let Us Know How BMT InfoNet Can Help YOU!

Visit our website: bmtinfonet.org

Email us: help@bmtinfonet.org

Give us call: 888-597-7674

We're here to help every step of the way!