Bone Health after Transplant

Celebrating a Second Chance at Life Survivorship Symposium

Joy Wu MD, PhD
Stanford University
School of Medicine

Joy Wu, MD, PhD
Associate Professor of Medicine
Division of Endocrinology

BMT InfoNet Survivorship Symposium
April 19, 2021
Take-home messages

- Bone loss is common after transplant
- Fractures due to osteoporosis are serious but preventable
- Risk of fracture depends on many factors
- Lifestyle changes can slow but not reverse bone loss
- When used properly, osteoporosis medications are safe and effective

What is osteoporosis?

- “Porous bone”
- A decrease in bone mass leading to increased fragility and risk of fracture
- 50% of women and 20% of men will suffer a fracture from osteoporosis
- ∼300,000 hip fractures per year
  - More than 20% will die within a year
  - Fewer than 50% will walk independently again

International Osteoporosis Foundation
World Osteoporosis Day 2012 report
Osteoporosis in perspective

Lifetime risk at age 50

**Women**
- 50% Fracture
- 12% Breast Cancer

**Men**
- 20% Fracture
- 17% Prostate Cancer

There are 5,500 fractures a day in the US due to osteoporosis…

Photo by J. Wu

2million2many.org

...that’s 2 million fractures a year.
Osteoporosis is a serious public health problem

Types of fractures

- Spine 27%
- Wrist 19%
- Hip 14%
- Pelvis 7%
- Other 33%

Bone loss after blood and marrow transplant

- Transplant recipients often have low bone mass even before transplant.
- Allogeneic transplant recipients can lose 6-9% of bone mass at the spine and 8-17% of bone mass at the hip in the first year after transplant.
- Bone loss occurs as early as 3 months after transplant.
Why are transplant recipients at risk for bone loss?

- Underlying disease leading to transplant
- Low estrogen or testosterone
  - Premature menopause after total body irradiation and/or chemotherapy
- Glucocorticoid treatment (for example for GVHD)
- Immunosuppression
- Radiation therapy
- Chemotherapy
- Other causes: heparin, kidney dysfunction, malabsorption, vitamin D deficiency

Weilbaecher, BBMT 2000

Rapid bone loss can occur after transplant

Gralow, JNCCN 2013
Bone loss after stem cell transplantation

- Massenkeil, Leukemia 2001
  - 67 adults undergoing allogeneic transplant
  - 49% had osteopenia or osteoporosis before transplant
  - 67% had osteopenia or osteoporosis 6 months after transplant

Bone loss is common in survivors of pediatric blood and marrow transplantation

- Increased fat tissue in bone marrow
- Spine fractures can be seen at a much younger age than usual

Mostoufi-Moab, JBMR 2015
Am I at risk for bone loss?

- Older age
- Lower bone density
- Previous fracture
- Glucocorticoid treatment
- Family history of osteoporosis (especially a parent with a hip fracture)
- Low body weight
- Tobacco use
- Excessive alcohol
- Rheumatoid arthritis
- Secondary causes of osteoporosis

Who should have a bone density test?

- General recommendations (American Society for Bone and Mineral Research)
  - Women age 65 and older and men age 70 and older
  - Younger postmenopausal women and men ages 50–69 with clinical risk factors
  - Anyone with a low-trauma fracture after age 50
  - Adults with a condition (e.g., rheumatoid arthritis) or taking a medication (e.g., glucocorticoids) associated with bone loss
Evaluation of bone health after blood and marrow transplant

- Bone density (DXA) scan and fracture risk assessment (FRAX):
  - At 3 months, if not done before
  - At 3 months, if early high-dose glucocorticoid treatment was administered
  - After 1 year on treatment and every 1-2 years thereafter
What is a bone density scan?

Raisz, NEJM 2005

FRAX® Fracture Risk Assessment Tool

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Questionnaire:
1. Age (between 40 and 90 years) or Date of Birth
2. Sex
   - Male
   - Female
3. Weight (kg)
4. Height (cm)
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 (g/cm^2)

BMD: 27.4

The ten year probability of fracture (%) without BMD

- Major osteoporotic: 18%
- Hip fracture: 3.3%

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

Visit www.bmtinfonet.org
Fracture risk depends on BMD and age

Recommended treatment threshold

“Osteoporosis” by bone density

Fracture risk increases with the number of risk factors

Risk factors:
- Previous fracture
- Parental fracture
- Smoking
- Steroid use
- Rheumatoid arthritis
- Excessive alcohol

Treatment threshold
How can I improve my bone health?

- Get enough calcium and vitamin D
- Be physically active
- Reduce your risk of falls
- Maintain a healthy weight
- Do not smoke
- Limit alcohol use
- Talk with your doctor about medicines you are taking that could weaken bones

Surgeon General’s Report on Bone Health 2019

How much calcium?

- Goal 1000-1200 mg daily
- Dietary sources
  - Milk, 1 cup = 302 mg
  - Yogurt, 1 cup = 300 mg
  - Cheddar cheese, 1.5 oz = 306 mg
  - Fortified orange juice, 1 cup = 260 mg
  - Canned salmon, with bones = 181 mg
  - Cottage cheese, 1 cup = 138 mg
  - Broccoli, 1 cup = 90 mg
- Supplements
  - No more than 500 mg at a time
  - If you are taking acid blocking medication, calcium citrate is recommended
  - Otherwise, calcium carbonate is fine

Visit www.bmtinfonet.org
How much vitamin D?

- Vitamin D – goal 800-1000 IU a day
  - Vitamin D2 (ergocalciferol) is a plant-based supplement
  - Vitamin D3 (cholecalciferol) is produced in the skin, animal-based

Physical activity

- At least 150 minutes of moderate or 75 minutes of vigorous activity a week
- Strength training 2-3 times per week
  - Weights or resistance
- Balance and flexibility are also important
- National Osteoporosis Foundation recommendations:
  - [https://www.nof.org/preventing-fractures/exercise-to-stay-healthy/](https://www.nof.org/preventing-fractures/exercise-to-stay-healthy/)
Do I need medication for osteoporosis?

- Not on glucocorticoids for GVHD:
  - History of a fragility fracture after age 50
  - Postmenopausal women or men over 50 with osteoporosis on a bone density scan
  - Estimated 10-year risk:
    - Major osteoporotic fracture >20%
    - Hip fracture >3%

- On glucocorticoids for GVHD:
  - Age over 40
    - History of a fragility fracture after age 50
    - Postmenopausal women or men over 50 with osteoporosis on a bone density scan
    - Estimated 10-year risk:
      - Major osteoporotic fracture >10%
      - Hip fracture >1%
  - Age under 40
    - History of a fragility fracture
    - Severe osteoporosis or rapid bone loss
### Medications for treating osteoporosis

<table>
<thead>
<tr>
<th>Prevent bone breakdown:</th>
<th>Promote bone formation:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective estrogen receptor modulators (SERMs)</td>
<td>Teriparatide (PTH)</td>
</tr>
<tr>
<td>Bisphosphonates</td>
<td>Abaloparatide (PTHrP)</td>
</tr>
<tr>
<td>Denosumab (anti-RANKL MAb)</td>
<td>Romosozumab (anti-sclerostin MAb)</td>
</tr>
</tbody>
</table>

#### Osteoporosis medications used in transplant recipients

<table>
<thead>
<tr>
<th>Class</th>
<th>How it’s given</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral bisphosphonates:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Alendronate (Fosamax)</td>
<td>Weekly tablets (except Boniva which is monthly)</td>
<td>Safe and effective</td>
<td>Heartburn</td>
</tr>
<tr>
<td>• Risedronate (Actonel)</td>
<td></td>
<td></td>
<td>Cannot be used with kidney disease</td>
</tr>
<tr>
<td>• Ibandronate (Boniva)</td>
<td></td>
<td></td>
<td>Boniva has not been shown to reduce all fracture types</td>
</tr>
<tr>
<td>IV bisphosphonate:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Zoledronic acid (Reclast)</td>
<td>Intravenous infusion once a year</td>
<td>Convenient</td>
<td>Cannot be used with kidney disease</td>
</tr>
<tr>
<td>Anti-RANKL monoclonal antibody:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Denosumab (Prolia)</td>
<td>Injection every 6 months</td>
<td>Marked increase in BMD</td>
<td>No safety or efficacy data in HCT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Can be used with kidney disease</td>
<td>Trial is ongoing</td>
</tr>
</tbody>
</table>
Common concerns about medications

- “I prefer natural remedies to taking medication.”
- “I am very sensitive to medications.”
- “I’ve read that osteoporosis medications can be dangerous.”
- “I have a mother/sister/aunt/friend that took this medication and had an unpleasant side effect.”

What are the benefits vs. risks of treatment?

Modified from Adler, JBMR 2016
What are the benefits vs. risks of treatment?

Over 10,000 patient-years
Number of preventable fractures:

Number of cases of:

- Osteonecrosis of the jaw
- Atypical fractures (5 years)
- Atypical fractures (10 years)

In the appropriate patients, the benefits of 5 years of bisphosphonate treatment far outweigh the risk.

Take-home messages

- Bone loss is common after transplant
- Fractures due to osteoporosis are serious but preventable
- Risk of fracture depends on many factors
- Lifestyle changes can slow but not reverse bone loss
- When used properly, osteoporosis medications are safe and effective