Protect Your Bones after Transplant or CAR T-cell Therapy

Celebrating a Second Chance at Life Survivorship Symposium

April 27 – May 3, 2024

Sarah Keller MD, MA
Rheumatologist, Assistant Professor at the Cleveland Clinic Lerner School of Medicine
Disclosures

- I have no financial disclosures.
Agenda

- **Impact of BMT on bone health**
  - Why osteoporosis and bone density loss matter
  - How is osteoporosis diagnosed
  - How to protect your bones
    - Regular bone density screening
    - Vitamin D and calcium supplementation
    - Weight-bearing and muscle-strengthening exercise
    - Optimization of lifestyle factors
    - Treatment in select patients
Risk Factors for Bone Loss after Allogeneic BMT

- Induction and consolidation chemotherapeutic agents
- Glucocorticoids (e.g. dexamethasone, prednisone)
- Calcineurin inhibitors (e.g. tacrolimus, cyclosporine)
- Hypogonadism
- Total body irradiation
- Low body mass index (BMI)/rapid weight loss
- Prolonged immobilization
- Decrease in vitamin D/calcium
- Advanced age
Risk Factors for Bone Loss after Allogeneic/Autologous BMT

- Induction and consolidation chemotherapeutic agents
- Glucocorticoids (e.g. dexamethasone, prednisone)
- Calcineurin inhibitors (e.g. tacrolimus, cyclosporine)
- Hypogonadism
- Total body irradiation
- Low body mass index (BMI)/rapid weight loss
- Prolonged immobilization
- Decrease in vitamin D/calcium
- Advanced age

Impact of BMT on Bone Health: Glucocorticoids
Agenda

• Impact of BMT on bone health
• Why osteoporosis and bone density loss matter
• How is osteoporosis diagnosed
• How to protect your bones
  • Regular bone density screening
  • Vitamin D and calcium supplementation
  • Weight-bearing and muscle-strengthening exercise
  • Optimization of lifestyle factors
  • Treatment in select patients
Why Osteoporosis and Bone Density Loss Matter

- Osteoporosis affects more than 10 million US adults (80% of whom are women)
- The direct cost is $17 billion; however, the indirect cost is far greater
- There are more than 2 million fractures annually
- By diagnosing osteoporosis and preventing fractures, we can increase patient survival, improve quality of life and decrease the large direct and indirect costs of this disease
Osteoporosis and Bone Density Loss: Fractures

- A fracture occurs when a force (like a fall) is applied to osteoporotic bone
- The most dreaded osteoporotic fracture is the hip fracture
- Hip fractures are associated with increased morbidity and mortality, particularly in the first year following hip fracture
Hip Fractures

- There is a 20% excess mortality during the first year following a hip fracture in women, and up to 50% excess risk of death in men.
- Up to 40% of patients are no longer able to walk independently in the first year following hip fracture.
- Up to 25% of patients are no longer able to live independently and require long-term care.
- Up to 80% of patients are unable to carry out at least one independent activity of daily living following a hip fracture.
Vertebral Compression Fractures

- The most common fractures in osteoporotic patients
- Like hip fractures, vertebral compression fractures are also associated with significant morbidity and mortality
- 20% of patients who have a vertebral fracture will have a recurrent vertebral fracture within 1 year, and up to 40% within 3 years
- Patients with a vertebral fracture are at double the risk for a subsequent hip fracture

Agenda

• Impact of BMT on bone health
• Why osteoporosis and bone density loss matter
• **How is osteoporosis diagnosed**
• How to protect your bones
  • Regular bone density screening
  • Vitamin D and calcium supplementation
  • Weight-bearing and muscle-strengthening exercise
  • Optimization of lifestyle factors
  • Treatment in select patients
Bone Density: Key Component of Bone Strength

Bone strength = Bone density + Bone quality

- Standard BMD measurements
- Bone turnover
- Mineralization
- Microarchitecture
- Geometry
- Damage accumulation
Methods of Diagnosing Osteoporosis

- Bone mineral density (BMD) measurement: T-score ≤ -2.5
- Fragility fracture
  - Hip fracture (with or without BMD measurement)
  - Clinical vertebral, proximal humerus or pelvis fracture with osteopenia
- Incidental radiographic vertebral fracture
- FRAX score
  - Hip fracture risk ≥ 3% or major osteoporosis fracture ≥ 20%
Dual Energy X-ray Absorptiometry (DXA) Scan

- DXA scan measures bone density
- DXA scanner is a radiographic machine that produces high energy and low energy x-ray beams
- These beams are passed through the patient
- X-rays that are absorbed by bone are measured for each beam
- Bone density is determined based on energy differences between the two beams
- Radiation energy is detected and converted into an areal density (g/cm²)
How DXA is Obtained
When to Screen: General Population

- Screening guidelines vary
- Most groups recommend screening in women > 65
- National Osteoporosis Foundation:
  - Women > 65 and men > 70
  - Post-menopausal women and men 50-69, depending on risk factor profile
  - Post-menopausal women and men 50-69 with a fragility fracture as an adult

When to Screen: Daily Glucocorticoid Use

- Lower threshold to screen patients on glucocorticoids (GC)
- Recommendations vary by group
- American College of Rheumatology 2017 guidelines:
  - Perform fracture risk assessment of all patients on GC at the start of treatment
  - Screen adults ≥ 40 years by obtaining DXA within 6 months of starting GC
  - Screen adults < 40 years with by obtaining DXA if history of previous osteoporosis or other significant risk factors

Arthritis Rheumatol. 2017 Aug;69(8):1521-153
When to Screen: Transplant Population

• Ideally, a DXA should be obtained prior to transplant.

• Rate of bone density loss is highest in the first 3-6 months after BMT.

• Should get a repeat scan at least every two years if your bone density is in the:
  • osteoporosis range (T-score ≤ -2.5)
  • osteopenia range (T-score between -1.0 and -2.5)
Agenda

• Impact of BMT on bone health
• Why osteoporosis and bone density loss matter
• How is osteoporosis diagnosed
• How to protect your bones
  • Regular bone density screening
  • Vitamin D and calcium supplementation
  • Weight-bearing and muscle-strengthening exercise
  • Optimization of lifestyle factors
• Treatment in select patients
Get Bone Density Scans Every 2 Years

• Make sure your doctor or provider orders a bone density scan, if not before your transplant, then as soon as possible after transplant

• Follow up with regular bone density (DXA) scans every 2 years if your bone density is in the osteoporotic or osteopenic range

• If you are on steroids, you can get a DXA every year

• Many transplant centers work closely with a metabolic bone clinic, but if not, request to see an expert in metabolic bone health
Optimize Calcium Intake

- 1200-1500 mg of daily calcium (including dietary intake + supplement)
- Total daily intake may include both dietary sources (from dairy and leafy green vegetables) and supplements if necessary
- Calcium intake from supplements should be split at least twice a day to maximize absorption
Optimize Vitamin D Intake

- The NOF (National Osteoporosis Foundation) recommends 800 to 1000 international units (IU) of vitamin D per day for adults aged 50 years and older.
- Aim for vitamin D 25-OH D level of ≥30.
Weight-Bearing and Muscle-Strengthening Exercise

• Weight-bearing Exercise:
  • Running/jogging
  • Walking
  • Hiking
  • Jumping rope/jumping jacks
  • High-impact aerobics (step, Zumba)
  • Dancing
  • Stair climbing

• Muscle-strengthening Exercise
  • Lifting free weights
  • Using weight machines
  • Using elastic exercise bands
  • Lifting your own body weight (squats, lunges)
  • Functional moving (standing from sitting position)
  • Balance exercises
How Much Exercise?

• Aim for at least 3 times per week
• Start at a low level and progress slowly
• Exercising too vigorously may increase risk of injury, including fractures
Activities to Avoid

• Activities that:
  • put excessive force on forward flexion of the spine
    • Certain yoga or Pilates positions where you bend forward
  • increase the risk of falling
  • require sudden, forceful movement
  • require forceful twisting motion (unless the person is accustomed to such movement)
  • put undue force/pressure on the spine
    • Horse-back riding, extreme skiing, bungee jumping
• Be careful not to lift too much
Modify Risk Factors

- Advanced age
- Female sex
- Menopause
- Prior fracture
- Family history of osteoporosis and/or fracture
- Low body weight, weight loss

- Smoking, excessive alcohol and caffeine consumption
- Low sunlight exposure and/or low vitamin D intake
- Low calcium intake
- Medications (glucocorticoids, androgen deprivation agents, aromatase inhibitors, proton pump inhibitors etc.)
Some People Require Treatment

• Bone mineral density (BMD) measurement: T-score ≤ -2.5
• Fragility fracture
  • Hip fracture
  • Clinical vertebral, proximal humerus or pelvis fracture with osteopenia
• Incidental radiographic vertebral fracture
• Increased FRAX
• Long term prednisone use
Some People Require Treatment: Chronic Prednisone

• If you are on chronic prednisone (for more than 3-6 months) you may need to be treated with anti-osteoporosis medications

• Lack of consensus about which patients should receive therapy to prevent bone loss and fractures

• There are some guidelines for clinicians

• Prednisone > 7.5 mg daily for 3-6 months

• Duration of therapy may be as short as one year
Osteoporosis Medication

Nutrition
- Calcium
- Vitamin D
- Vitamin K2

Bone resorption
- Anti-resorption Drugs
  - Calcitonin
  - SERMs
  - BPs
  - Anti-RANKL

Bone formation
- Anabolic Drugs
  - PTH
  - Sclerostin inhibitors
## Effect of Osteoporosis Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Does/Frequency</th>
<th>Fracture Risk Reduction (in post-menopausal osteoporosis)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisphosphonates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alendronate</td>
<td>70 mg by mouth weekly</td>
<td>35-65% Vertebral 23% Non-vertebral 45-55% Hip</td>
<td>Can cause hypocalcemia and esophagitis.</td>
</tr>
<tr>
<td>Risedronate</td>
<td>35 mg by mouth weekly</td>
<td>41% Vertebral 39% Non-vertebral 30% Hip</td>
<td>Can cause hypocalcemia and esophagitis.</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>150 mg by mouth monthly</td>
<td>62% Vertebral</td>
<td>Can cause hypocalcemia and esophagitis. No evidence of hip fracture protection</td>
</tr>
<tr>
<td>Zoledronate</td>
<td>5 mg IV annually</td>
<td>70% Vertebral 25% Non-vertebral 41% Hip</td>
<td>Can cause hypocalcemia. 32% have an acute phase reaction with their first infusion consisting of fever, myalgias and flu-like symptoms lasting 24-72 hours [55]</td>
</tr>
</tbody>
</table>
# Effect of Osteoporosis Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Does/Frequency</th>
<th>Fracture Risk Reduction (in post-menopausal osteoporosis)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raloxifene Evista</td>
<td>60 mg by mouth daily</td>
<td>30% Vertebral</td>
<td>No data for hip fracture prevention</td>
</tr>
<tr>
<td>Denosumab Prolia and Xgeva</td>
<td>60 mg subcutaneously every 6 months</td>
<td>68% Vertebral, 20% Non-vertebral, 40% Hip</td>
<td>Can cause hypocalcemia and musculoskeletal pain. Cannot be stopped/delayed due to increased risk of multiple rebound vertebral compression factors [58]</td>
</tr>
<tr>
<td>Teriparatide</td>
<td>20 mcg subcutaneously daily x 2 years</td>
<td>65% Vertebral, 40% Non-vertebral</td>
<td>Contraindicated if history of radiation. Must be followed by anti-resorptive therapy to avoid loss of bone marrow density gains</td>
</tr>
<tr>
<td>Abaloparatide</td>
<td>80 mcg subcutaneously daily x 2 years</td>
<td>86% Vertebral, 43% Non-vertebral</td>
<td>Contraindicated if history of radiation. Must be followed by anti-resorptive therapy to avoid loss of bone mineral density gains</td>
</tr>
<tr>
<td>Romosozumab Evenity</td>
<td>210 mg subcutaneously Monthly x 1 year</td>
<td>73% Vertebral</td>
<td>Contraindicated if history of heart attack or stroke in the past year. Must be followed by anti-resorptive therapy to avoid loss of bone mineral density gains</td>
</tr>
</tbody>
</table>
Summary

• Impact of BMT on bone health
• Why osteoporosis and bone density loss matter
• How is osteoporosis diagnosed
• How to protect your bones
  • Regular bone density screening
  • Vitamin D and calcium supplementation
  • Weight-bearing and muscle-strengthening exercise
  • Optimization of lifestyle factors
  • Treatment in select patients
Questions?

Sarah Keller MD, MA
Rheumatologist, Assistant Professor at the Cleveland Clinic
Lerner School of Medicine.
Let Us Know How We Can Help You

Visit our website:  bmtinfonet.org

Email us: help@bmtinfonet.org

Phone: 888-597-7674 or 847-433-3313

Find us on:

Facebook,  facebook.com/bmtinfonet