Bone Health and Other Endocrine Issues after Transplant or CAR T-cell Therapy

Celebrating a Second Chance at Life Survivorship Symposium

May 3-9, 2025

Angeliki Stamatouli, MD
Virginia Commonwealth University

Bone Health after Stem Cell Transplant

Angeliki Stamatouli MD

Assistant professor of Internal Medicine-Endocrinology
Massey Cancer Center-Virginia Commonwealth University

Celebrating a second chance at life
Survivorship Symposium
May 3-9, 2025

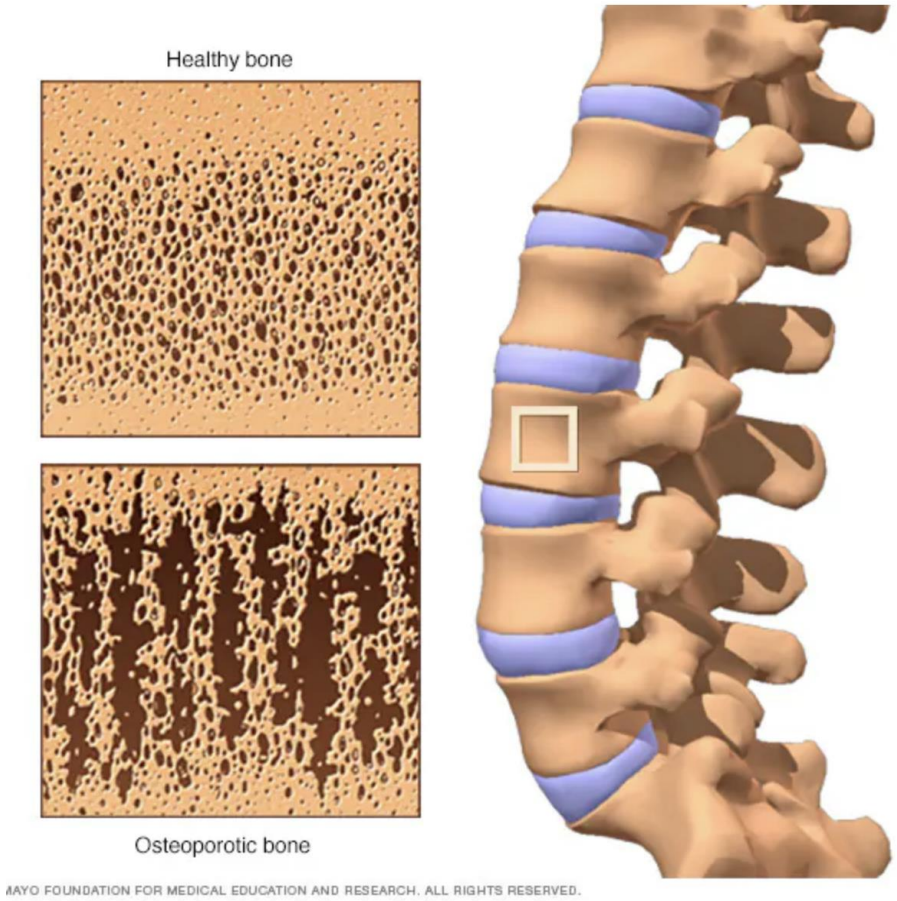
No financial Disclosures

What We Will Discuss:

- Define low bone mass/osteoporosis
- Bone health after transplant
- Risk factors for bone loss after transplant
- Monitoring bone health after transplant
- Diet and lifestyle interventions to improve bone mass
- Treatment for osteoporosis

What is “Osteoporosis”?

- **"Osteo" (Greek):** means "bone".
- **"Poros" (Greek):** means "pore" or "passage," indicating holes or spaces.
- **Osteoporosis:** The combination of these two Greek words indicates a condition where bones become porous or full of holes. This makes to bone be more likely to fracture.



Picture: https://www.mayoclinic.org/diseases-conditions/osteoporosis/symptoms-causes/syc-20351968

Osteoporosis in North America

- One in two women and one in four men over age 50 will have a fracture due to osteoporosis
- Each year in the USA, approximately 300,000 hip fractures occur.
  - One in four die in the year following the fracture
  - One in four move from the hospital to a nursing home and never return home
  - One in two never regain their previous function
- Annual fractures are projected to increase from 1.9 million to 3.2 million, 2018 to 2040, with related costs rising from $57 billion to over $95 billion USD annually

What are the Symptoms of Osteoporosis?

- Osteoporosis is a “silent” disease
- Symptoms are usually related to complications
  - Fractures with minimal trauma
  - Height loss
  - Pain due to a broken bone, e.g. back pain or tenderness
  - Changes in posture
  - Loss of mobility

Bone Loss Associated with Stem Cell Transplant

Bone Loss	Lumbar Spine BMD Loss at 1 Year (%)
Bone loss associated with normal aging	
Men	0.5
Late menopause women	1.0
Early menopause women	2.0
Cancer treatment–induced bone loss	
AI therapy	2.6
Bone marrow transplantation	3.3
ADT	4.6
AI therapy plus GnRH therapy	7.0
Ovarian failure secondary to chemotherapy	7.7

Bone loss after stem cell transplant (SCT) increases the risk of fragility fractures

- 50-75% after allogeneic SCT
- 20-65% after autologous SCT
- 3-6 months after SCT

Clin Oncol 37:2916-2946. © 2019 by American Society of Clinical Oncology
Guise TA: Oncologist 11:1121-1131, 2006
M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802

Risk Factors for Bone Loss in Stem Cell Transplant (SCT) Patients

Genetic Factors and Other Medical Conditions

- Age
- Race
- Sex ()
- Menopause
- Family or personal history of fragility fracture
- Low Body weight

- Osteoporosis due to endocrine disorders (eg elevated cortisol, elevated parathyroid hormone)
- Rheumatoid arthritis and other autoimmune conditions
- Chronic kidney disease
- Chronic liver disease
- Sickle cell
- Multiple myeloma

Clin Oncol 37:2916-2946. © 2019 by American Society of Clinical Oncology
M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802

Lifestyle

- Current cigarette smoking
- Excessive alcohol consumption (≥3 drinks/day)
- Sedentary lifestyle

Clin Oncol 37:2916-2946. © 2019 by American Society of Clinical Oncology
M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802

Cancer and Cancer Treatments

- Chemotherapy
  - Toxic to osteoblasts and bone marrow cells
  - Menopause in women
  - Low testosterone in men
- Radiation
- Use of glucocorticoids (prednisone, dexamethasone etc) for >3-6 months
- Calcineurin inhibitors (eg tacrolimus)

Clin Oncol 37:2916-2946. © 2019 by American Society of Clinical Oncology
M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802

Other Factors

- Malnourishment due to
  - Nausea
  - Cancer cachexia (significant loss of body weight, including loss of muscle mass and fat in a person who is not trying to lose weight)
- Cancer-related fatigue → reduced physical activity, muscle and bone loss
- Graft versus Host disease
- Iron overload

Clin Oncol 37:2916-2946. © 2019 by American Society of Clinical Oncology
M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802

How should we monitor bone health after a stem cell transplant?

Dual-energy x-ray absorptiometry (DXA)

What is a DXA Scan?

- A medical imaging test that measures bone mineral density
- A non-invasive procedure used to assess bone health that is particularly useful in diagnosing conditions like osteoporosis.
- The DXA scan helps us understand the risk of fractures and monitor any changes in bone density over time.

What to Expect During a DXA Test

- During the scan, the patient lies on a padded table while a machine passes over the body. The scan is painless and typically takes 10 to 20 minutes.
- The amount of radiation used in a DXA scan is very low, much less than a standard chest X-ray, making it a safe procedure.
- Patients can eat normally on the day of the test, but they may need to avoid taking calcium supplements for 24 hours before the scan.
- Patients should wear comfortable clothing without metal zippers or buttons.

Understanding DXA Scan Results: T-Score

After the DXA scan, the patients receive a report that includes a few key numbers and terms. Here's what they mean:

T-Score:

The T-score compares the bone density to the average peak bone density of a healthy young white female.

- A T-score of **-1.0 or above** is considered normal.
- A T-score between **-1.0 and -2.5** indicates low bone density, or osteopenia.
- A T-score of **-2.5 or lower** suggests osteoporosis, meaning the bones are more fragile and at higher risk for fractures.

Understanding DXA Scan Results: Z-Score

Z-Score (< 50 years old):

- The Z-score compares the bone density to what is expected for someone of the same age, gender, and size.
- A Z-score below -2.0 may suggest that something other than aging is causing bone loss, and further investigation might be needed.

FRAX® Fracture Risk Assessment Tool

Home | Calculation Tool | Paper Charts | FAQ | References | CE Mark | English

Calculation Tool

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

Country: US (Caucasian) Name/ID: About the risk factors

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth
   Age: 65 Date of Birth: Y: M: D:
2. Sex — Male / Female
3. Weight (kg) — 85
4. Height (cm) — 170
5. Previous Fracture — No / Yes
6. Parent Fractured Hip — No / Yes
7. Current Smoking — No / Yes
8. Glucocorticoids — No / Yes
9. Rheumatoid arthritis — No / Yes
10. Secondary osteoporosis — No / Yes
11. Alcohol 3 or more units/day — No / Yes
12. Femoral neck BMD (g/cm^2) — Select BMD: 0.689

Clear | Calculate

BMI: 29.4
The ten year probability of fracture (%)

without BMD

Major osteoporotic	10
Hip Fracture	2.1

Weight Conversion

Pounds → kg

Convert

Height Conversion

Inches → cm

Convert

13367916
Individuals with fracture risk assessed since 1st June 2011

Additional Evaluation During Visits

- Frequent visits –discussion of complications with the provider
- Helpful blood tests
- X-ray spine to evaluate for fractures

Diet and Lifestyle Interventions to Improve Bone Density or Prevent Bone Loss

- Optimize calcium intake
- Goal:
  - daily calcium intake 1000-1200 mg from diet (preferred) and supplements

https://www.health.harvard.edu/nutrition/calcium-rich-foods-how-to-boost-your-intake-of-this-important-mineral

MILK & MILK DRINKS

Food (1 cup)	Calcium (mg)
Milk, semi-skimmed	294
Milk, skimmed	299
Milk, whole	289
Milkshake	441
Sheep Milk	466
Soy Drink (non-enriched)	32
Soy Drink (calcium-enriched*)	294
Rice Drink (non-enriched)	27
Oat Milk (non-enriched)	20
Almond Milk (non-enriched)	110

YOGHURT

Food (1 cup)	Calcium (mg)
Yoghurt, flavoured	322
Yoghurt, with fruit pieces	276
Yoghurt, natural	338

CHEESE

Food	Serving	Calcium (mg)
Hard Cheese (e.g. Cheddar, Parmesan, Emmental, Gruyère)	1 oz	224
Fresh Cheese (e.g. Cottage Cheese, Riccotta, Mascarpone)	1 cup	156
Soft Cheese (e.g. Brie, Camembert)	1 oz	112
Feta	1 oz	126
Mozzarella	1 oz	113
Cream Cheese	1 tbsp	15

CREAM & DESSERTS

Food	Serving	Calcium (mg)
Cream, double, whipped	1 fl. oz	21
Cream full	1 fl. oz	21
Custard made with milk, vanilla	1/2 cup	130
Ice Cream, vanilla	1/2 cup	82
Pudding, vanilla	1 container (3 1/2 oz)	97
Rice Pudding	1/2 cup	131
Pancake	3 pancakes (3 3/4 oz)	81
Cheesecake	1 slice (3 oz)	55
Waffle, round, 7" diameter	1 waffle, (2 2/3 oz)	44

MEAT, FISH AND EGGS

Food	Serving	Calcium (mg)
Egg	1 large (1 3/4 oz)	27
Red Meat	3 oz	5
Chicken	3 oz	12
Fish (e.g. Cod, Trout, Herring, Whitebait)	3 oz	14
Tuna, canned	3 oz	24
Sardines in Oil, canned	1 can (3 3/4 oz)	368
Smoked Salmon	3 oz	13
Shrimp	3 oz	26

FRUITS

Food	Serving	Calcium (mg)
Orange	1 fruit (2 5/8" dia)	52
Apple	1 medium (3" dia)	9
Banana	1 medium (7" to 7 7/8" long)	9
Apricot	1 fruit	5
Currant (dried gooseberry)	1 cup	86
Figs, dried	1 cup	238
Raisins (dried grapes)	1 oz (60 raisins)	22

VEGETABLES

Food	Serving	Calcium (mg)
Lettuce	1 cup	14
Kale, Collard Greens	1 cup (raw)	13
Bok Choy/Pak Choi	1 cup (raw)	28
Gombo/Okra	1 cup (raw)	64
Cress	1 cup (raw)	78
Rhubarb	1 cup (raw, sliced)	105
Carrots	1 cup (raw sliced)	37
Tomatoes	1 cup (raw chopped)	17
Broccoli	1 cup (raw chopped)	85

BEANS & LENTILS

Food	Serving	Calcium (mg)
Lentils	1/2 cup raw	48
Chick Peas	1/2 cup raw	124
White Beans	1/2 cup raw	167
Red Beans	1/2 cup raw	107
Green/French Beans	1 cup	7

STARCHY FOODS

Food	Serving	Calcium (mg)
Pasta (cooked)	1 cup	17
Rice, White (boiled)	1 cup	4
Potatoes (boiled)	1 cup	9
White Bread	1 slice (oz)	4
Wholemeal Bread	1 slice (oz)	8
Muesli (cereals)	2/3 cup	23
Naan	1 piece (3 oz)	68

NUTS & SEEDS

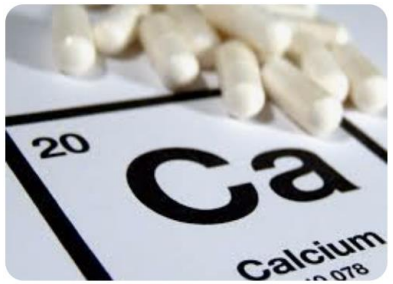
Food	Serving	Calcium (mg)
Almonds	1 oz	70
Walnuts	1 oz	26
Hazelnuts	1 oz	52
Brazil Nuts	1 oz	26
Sesame Seeds (hulled)	1 tbsp	11
Tahini Paste	1 tbsp	21

PROCESSED FOODS

Food	Serving	Calcium (mg)
Quiche (cheese, eggs)	1 piece (1/8 of 9" dia)	203
Omelet with Cheese	2 oz (1 egg)	127
Pasta with Cheese	1 cup	337
Pizza, (3 3/4 oz, 1/8 of 14" dia pizza)	1 slice	135
Lasagna	1 cup	171
Cheeseburger	1 large (10 oz)	256

OTHERS

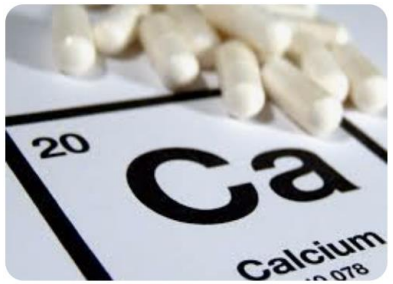
Food	Serving	Calcium (mg)
Tofu	1/2 cup	132
Seaweed	2 tbsp	7
Wakame	2 tbsp	15



Calcium Supplementation

- Supplementation is advised for people who cannot get enough calcium through their diet.
- The two main forms of calcium in supplements are carbonate and citrate.
  - Calcium carbonate is more commonly available and is absorbed most efficiently when taken with food.
  - Calcium citrate is absorbed equally well when taken with or without food.

Clin Oncol 37:2916-2946. © 2019 by American Society of Clinical Oncology
M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802



Calcium Supplementation: Caution

- Caution with calcium supplement intake (500-600 mg/day), as high intake of supplements could increase the risk for kidney stones
- For patients with malabsorption or on proton pump inhibitors, calcium citrate is suggested for better absorption.

Clin Oncol 37:2916-2946. © 2019 by American Society of Clinical Oncology
M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802

Vitamin D Supplementation

- Vitamin D supplementation is crucial for both health:
  - Helps with calcium absorption from food in the intestine
  - Helps with bone mineralization
  - Reduces the risk of falling
- Daily recommended dose: 1000-2000 units per day or to maintain levels of 25 hydroxy vitamin D of 20-50 ng/ml (personal recommendation >30 ng/ml)

M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802

Food Rich in Vitamin D

Food	Vitamin D content (IU) *
Wild Salmon	600-1000
Farmed Salmon	100-250
Sardines, canned	300-600
Tuna, canned	236
Shitake mushrooms, fresh	100
Shitake mushrooms, sun-dried	1600
Egg Yolk	20 per yolk

*per 100 mg unless otherwise stated

IU: International Unit

The Role of Exercise

- Improves strength, posture, balance
- Decreases risk for falls
- A physical therapy evaluation is suggested for all patients after transplant to individualize their exercise plan (type of exercise, intensity)
  - Weight-bearing exercise (jumping, skipping, bench stepping)
  - Resistance exercise (weight- training, pushups, resistance band exercise)
  - Avoid forward bending and lifting weights over 10 lbs over head

M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802

General Lifestyle Recommendations

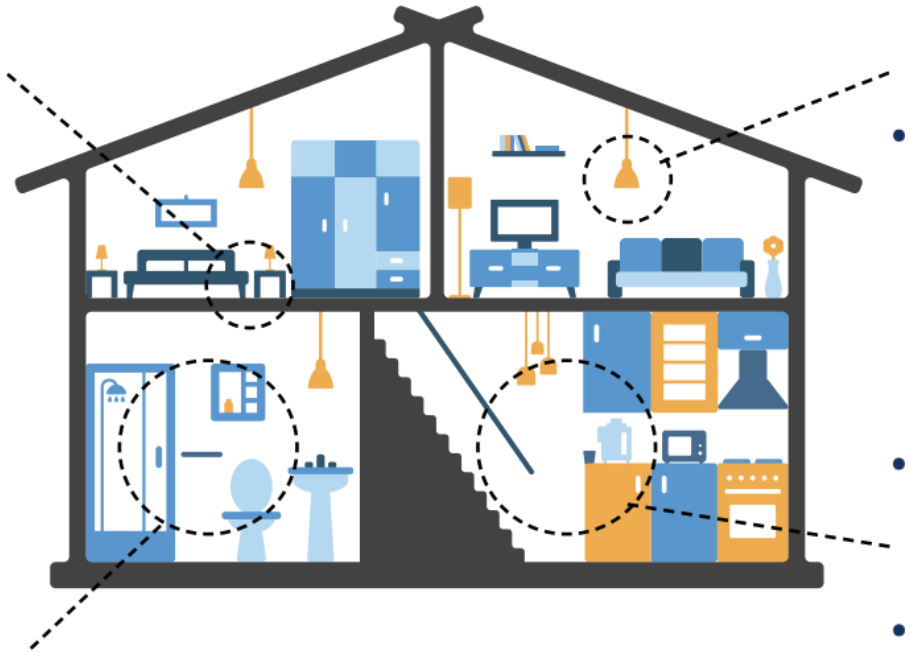
- Balanced diet: low carbohydrate/ high protein
- Smoking cessation
- Limit alcohol intake (≤2 drinks per day)
- Lowest dose of prednisone/steroids
- Maintain good vision

M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802

HOW TO FALL-PROOF YOUR HOME

PLEASE ASK FOR HELP FROM FAMILY, FRIENDS, NEIGHBOURS OR CARERS SO THAT CHANGES CAN BE MADE SAFELY!

- **Remove objects** you could trip over
- Ensure mats are firmly affixed, **repair loose carpet** or raised areas on the floor
- Move furniture out of walking paths
- **Be aware** of raised doorways and steps
- Use **non-skid floor wax**



- Keep your home **well lit**, especially hallways, stairways, and outside walkways
- Add extra light switches or use lights triggered by **motion sensors**

- Always **hold on to handrails** and ensure they are stable and secure

- Install **handrails** by the bathtub or shower
- Have **non-skid mats** (and watch out for slippery, wet surfaces)

- **Wipe up** any spills immediately
- Keep regularly used kitchen items at an **easy-to-reach level**

When Should We Start Treatment?
Patients Who Have Not Received Glucocorticoids

- History of fragility fractures age ≥50 years
- Postmenopausal women and men age ≥50 years with femoral neck, total hip, or lumbar spine T-score ≤-2.5.
- Patients age 40-90 years with T-score between -1.0 and -2.5 and FRAX* 10-year probability for major osteoporotic fracture ≥ 20% or 10-year risk of hip fracture ≥3%

M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802

When Should We Start Treatment?
Patients Who Received Glucocorticoids ≥ Age 40

Adults age ≥40 years
• History of fragility fractures • Men aged ≥ 50 years and postmenopausal women with femoral neck, total hip, or lumbar spine T-score ≤-2.5 • FRAX* (glucocorticoid-adjusted‡) 10-year probability of major osteoporotic fracture† ≥10% • FRAX* (glucocorticoid-adjusted‡) 10-year probability of hip fracture > 1%

M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802

When Should We Start Treatment?
Patients Who Received Glucocorticoids < Age 40

Adults age <40 years
• History of fragility fractures • Hip or lumbar spine Z-score <-3.0 or rapid bone loss (≥10% at the hip or lumbar spine over 1 year) AND Continuing glucocorticoids treatment at a prednisone dose of ≥7.5 mg/day or equivalent for ≥6 months

M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802

Osteoporosis Medications

The primary goal of osteoporosis medications is to strengthen the bones and reduce fracture risk.

Antiresorptives	Anabolic	Hormonal
They slow down the bone-resorbing cells (osteoclasts), which break down old bone, allowing the bone-building cells (osteoblasts) to work more effectively, thus strengthening bones and reducing fracture risk	They stimulate bone formation leading to stronger bones and decreased fracture risk	May improve bone density when estrogen and testosterone levels are low in women and men respectively

Osteoporosis Medications

Antiresorptives	Anabolic	Hormonal

• Bisphosphonates
  • Oral (eg alendronate, risendronate)
  • Intravenous (eg Zolendronic acid)
• Denosumab SC
	• PTH receptor agonists: Teriparatide, Abaloparatide
	• Romosozumab
		• Raloxifene
		• Estrogen (females)
		• Testosterone (males)

Antiresorptive Medications

- First-line therapy for prevention and treatment of osteoporosis in SCT patients
- They are important for myeloma therapy before and after SCT
- Calcium and vitamin D levels should be at goal before and during treatment to prevent low calcium levels a few days after the administration of the medications

Antiresorptive Medications - Toxicities

- Oral bisphosphonates can cause inflammation of the esophagus
- IV Zolendronic acid can cause flu-like reaction after administration
- Oral bisphosphonates and IV Zolendronic acid are not safe in patients with advanced kidney disease; denosumab is safe.
- Denosumab should be given every 6 months. Delay or discontinuation of the medication could increase the risk of fractures/ worsen bone density

Antiresorptive Medications:
Atypical Femoral Fractures

- Late onset, rare complication (more common with bisphosphonate)
- Common in oncology patients
- Limit bisphosphonate use to 3-5 years

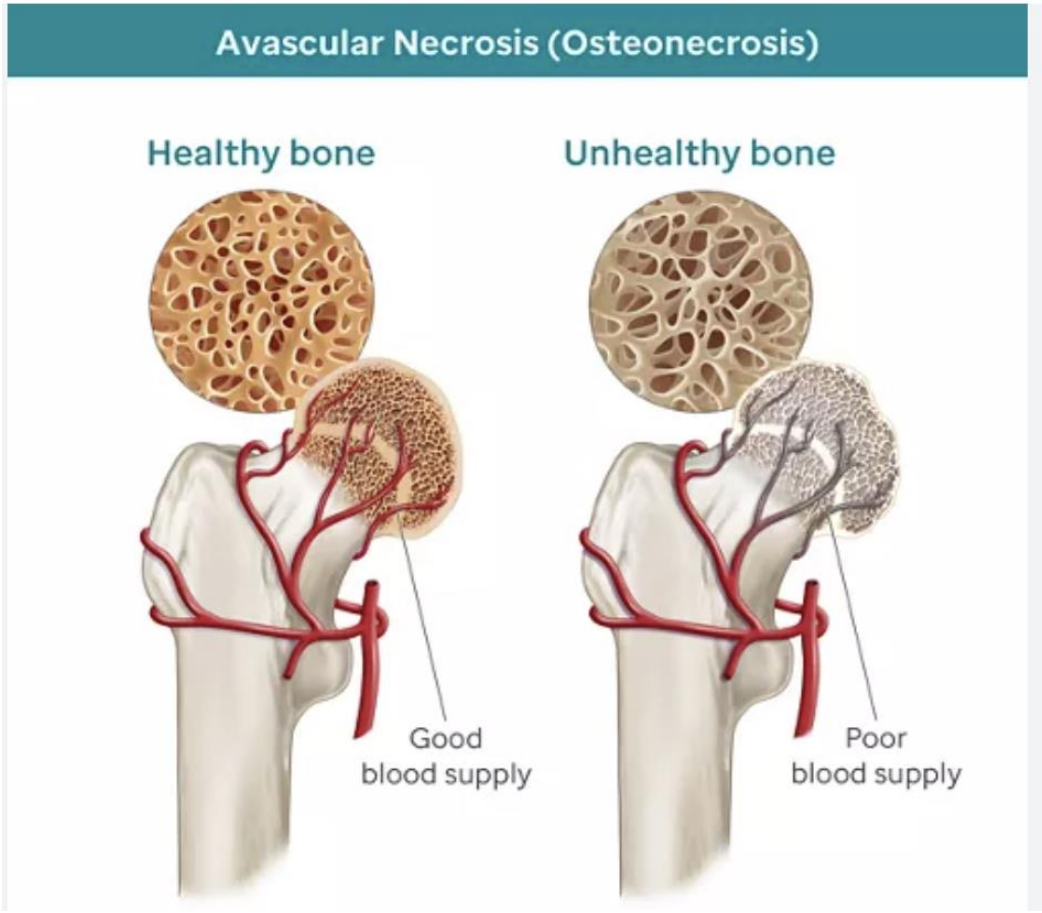
Dent. J. **2023**, *11*(4), 104
https://www.researchgate.net/publication/308758629_Clinical_features_of_an_atypical_femur_fracture

Antiresorptive Medications
Osteonecrosis of the Jaw

- Late onset, rare complication
  - (more common with denosumab)
- Common in oncology patients
- Comprehensive dental exam and elimination of oral infections before starting anti-resorptive treatment is essential

Dent. J. **2023**, *11*(4), 104
https://www.researchgate.net/publication/308758629_Clinical_features_of_an_atypical_femur_fracture

Avascular Necrosis After Transplant



Diagnosed the first 2 years after stem cell transplant (SCT)

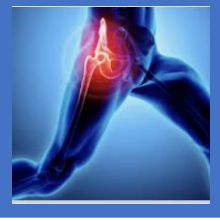
- 5-19% in allogeneic SCT
- 2-4% in autologous SCT

https://together.stjude.org/en-us

M. Bar et al. / Biol Blood Marrow Transplant 26 (2020) 1784 1802

Symptoms of Avascular Necrosis

Joint pain when moving



Joint pain at rest

Limited range of motion

Summary

- Bone loss is common after SCT
- There are multiple risk factors (genetic, lifestyle, cancer treatments) that are associated with bone loss
- Regular monitoring for bone loss is essential before and after SCT
- Dietary modification and lifestyle changes are crucial to prevent bone loss and improve bone health
- Bisphosphonates are the treatment of choice for managing osteoporosis

Questions?

Angeliki Stamatouli, MD
Virginia Commonwealth University

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