Beyond the Break

After Breast Cancer:
Osteoporosis in Survivorship

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Disclosures

- No disclosures
Osteoporosis in Breast Cancer Survivorship
(Early stage disease without evidence of recurrence)

Objectives

1. To understand Cancer-Treatment-Induced Bone Loss (CTIBL) and its impact

2. To understand how osteoporosis happens

3. To know how and when to treat osteoporosis in this special population

4. To know the surveillance protocol
In Canada ....

26,000 diagnosed yearly with breast Cancer

90% of these women are treated for curable disease

Cancer-Treatment-Induced Bone Loss in now a recognized entity

70% of breast cancers are treated with hormonal therapy
“It’s not about us without us”
A patient story

• 43yo breast cancer survivor
• Just post chemotherapy FEC-T
• ER-PR positive tumor stage 2 node positive
• BRCA positive, oophorectomy
• Just started aromatase inhibitor
1 in 5 women will sustain an Aromatase Inhibitor – related fracture over 5 years

10 years of AI treatment increased that risk by 2-3%
Osteoporosis

Healthy Bone

Bone with Osteoporosis
Pathogenesis of Osteoporosis

Estrogen, Vitamin D
PTH, Smoking
Chemotherapy, Renal disease
Malabsorption, Glucocorticoids
Medications PPI, Dilantin
Hyperthyroid, Rheumatoid Arthritis

Remodelling

Osteoclast

Rank receptors

Osteoblast

Osteoblasts produce fibrous collagen
This mineralizes to bone

H+ ions dissolve the structural hydroxyapatite
Let’s understand Cancer-Treatment-Induced Bone Loss
Cancer-Treatment-Induced Bone Loss (CTIBL)
Tamoxifen

- Used in pre-menopausal ER+ women to decrease the risk of systemic relapse
- Ovarian estrogen production continues and only inhibited at breast site
- It is a selective estrogen response modifier: it acts like an anti-estrogen in breast tissue, but acts like estrogen in the bone and protects against osteoporosis
- Risks include blood clot (<1%) and endometrial cancer (<2%)
- Other side effects include: hot flashes, night sweats, mood swings and vaginal dryness
Aromatase Inhibitors (AIs)

- Used in post-menopausal ER+ women to decrease the risk of systemic relapse
- Anastrazole (Arimidex®), exemestane (Aromasin®), letrozole (Femara®)
- Inhibit the enzyme aromatase from converting androgens into estrogen
- Do not block the production of estrogen from the ovaries therefore must be menopausal to use this
Fragility Fracture
3 months later in a fall on ice
Does she need Antiresorptive Therapy?
How Do We Treat This Problem in Survivorship?

The decision to start therapy should also take into account:

- Treatment history and ongoing anti-hormonal drugs
- Skeletal radiation
- Risk of bone metastases /recurrence
- BMD
- Risk of fracture – multifactorial
- Life expectancy
- Benefits of treatment
- Side effects of treatment
- Risk of harm
Baseline BMD

The clinical diagnosis of osteoporosis: a position statement from the National Bone Health Alliance Working Group

Treatment Decisions in Breast Cancer Patients

- Bone-directed therapy should be given to all patients with a T-score < −2.0
- or with a T-score of < −1.5 SD with one additional RF,
- or with ≥2 risk factors (without BMD) for the duration of AI treatment.
- Patients with T-score > −1.5 SD and no risk factors should be managed based on BMD loss during the first year and the local guidelines for postmenopausal osteoporosis

*J Bone Oncol*. 2017 Jun; 7: 1–12
Using FRAX = Add Rheumatoid Arthritis Risk for CTIBL risk (systemic chemo/AI)
Other Factors in Breast Cancer Treatment contributing to Osteoporosis Treatment Decision

• Peripheral neuropathy with increased risk of falls
  Platinums, Taxanes, including docetaxel (Taxotere) and paclitaxel (Taxol) Vincristine, vinblastine, Bortezomib (Velcade)
• Radiation therapy. Radiation therapy may damage nerves. Symptoms may take years to appear.
• Surgery. Lung or breast surgery may lead to neuropathy

• Inactivity – illness and chemotherapy treatment
• Use of steroids in history of treatment of cancer / chemo
• Malnutrition lack of adequate Ca & vit D during treatment
Now FRAX calculates.....
Discussion of Osteoporosis Agents

**Bisphosphonates:** First line therapy in CTIBL / osteoporosis in breast cancer survivorship. IV Zoledronic acid or PO Alendronate, risedronate, clodronate

**Demosumab** is an antibody to RANKL disabling the osteoclast activation

**Hormonal Agents:** The use of estrogens in breast cancer patients, even if the tumor is ER neg is controversial. Raloxifene but not concurrent with **Tamoxifen** due to adverse estrogen receptor modulation. BMD modulation has benefit but fracture risk unclear.

**Calcitonin i/n** dec vertebral #s but not non-vertebral

**Teriparatide** (human recomb PTH) RELATIVE CONTRAINDICATION in women with a history of Breast Cancer – anabolic bone mechanism activates non-clinical micro-metastases and may cause osteosarcoma in radiation therapy patients.
Cancer-Treatment-Induced Bone Loss (CTIBL)

- **Cyclophosphamide**
- **Doxorubicin**
- **Methotrexate**

**Estrogen depletion**
**Ovarian dysfunction**

**Tamoxifen & AI**

**Demosumab**

**Bisphosphonates**

- Dissolve the structural hydroxyapatite

**Osteoblasts**
- Produce fibrous collagen
- This mineralizes to bone

**Osteoclast**
- Acidic environment
- Dissolve bone matrix

**Rank receptors**

**RANKL**
ASCO 2017 Management of Aromatase Inhibitor–Associated Bone Loss in Postmenopausal Women With Hormone-Sensitive Breast Cancer

- 6-monthly denosumab or yearly zoledronic acid for the duration of aromatase inhibitor therapy is recommend for the prevention of aromatase inhibitor–associated bone loss in postmenopausal women receiving adjuvant aromatase inhibitor therapy, with zoledronic acid recommended when effects on disease recurrence are the priority and denosumab recommended when fracture risk is the dominant concern.

- Because of the decreased incidence of bone recurrence and breast cancer–specific mortality associated with bisphosphonate use, adjuvant bisphosphonates are recommended for all postmenopausal women at significant risk of disease recurrence.

- Compliance should be regularly assessed as well as bone mineral density after 12 to 24 months on treatment.
She starts taking Oral Bisphosphonate therapy

Not wanting infusion, she agrees on Alendronate
She experiences side effects including
upset stomach, dizziness

She discontinues the Alendronate
and asks to consider other therapy
She decides to take Denosumab

She takes 60 mg S/Q Q 6 months
Bloodwork is checked before her injection:

- TSH 2.1
- Calcium – adjusted 2.75
- PTH 6.5
- Cr 75
- Egfr 78
- Vitamin D 102
- Hb 120
Common Secondary Causes of Osteoporosis

- Hyperthyroid – 1ry or 2ndry
- Primary Hyperparathyroidism
- Vitamin D deficiency
- Malabsorption – celiac
- Alcoholism
- Diabetes Type 1
- Rheumatoid arthritis
- COPD

- Phenobarbital, steroids
- Osteogenesis imperfecta
- hyperprolactinemia
- Myeloma, some carcinomas
- Chronic renal disease
- Pregnancy
- Anorexia nervosa
- Chronic liver disease
- Marfans syndrome
- Ehlers-Danlos syndrome
Survivorship Surveillance Summary in all patients initiating aromatase inhibitors  

- fracture risk FRAX should be assessed
- exercise and calcium/vitamin D supplementation.
- Bone-directed therapy should be recommended for the duration of Al treatment to all patients with
  - a T score less than –2.0
  - or with a T score less than –1.5 with 1 additional risk factor,
  - or with 2 or more risk factors (without BMD)
  - Patients with a T score greater than –1.5 and no risk factors should be managed based on BMD loss during the first year and based on local guidelines for postmenopausal osteoporosis.

- 6-monthly denosumab or yearly zoledronic acid for the duration of aromatase inhibitor therapy is recommend for the prevention of Al bone loss in postmenopausal women when effects on disease recurrence are the priority and

- Denosumab recommended when fracture risk is the dominant concern.

- PREVENTION: Because of the decreased incidence of bone recurrence and breast cancer–specific mortality associated with bisphosphonate use, adjuvant bisphosphonates are recommended for all postmenopausal women at significant risk of disease recurrence.

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Thanks for listening today
Questions?