Royal Brisbane and Women's Hospital

2023

6th Annual

CANCER PRECEPTORSHIP

FOR GENERAL PRACTITIONERS

Metro North Health | Queensland Government

Bone Health and Early Breast Cancer in Females

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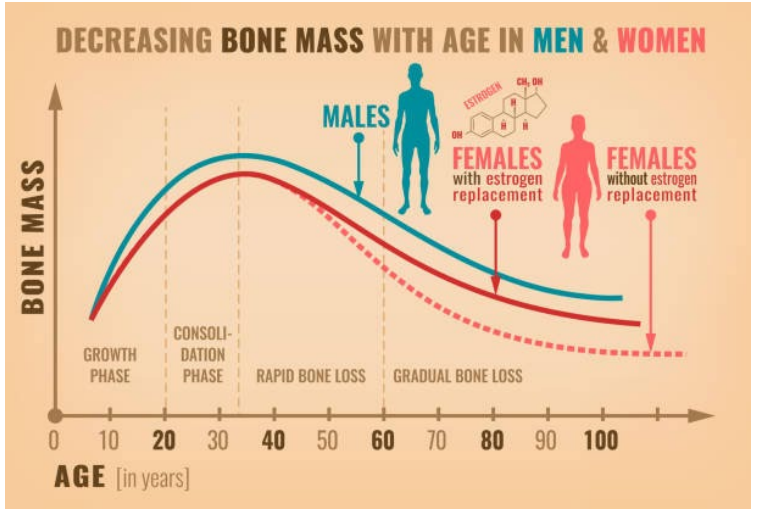
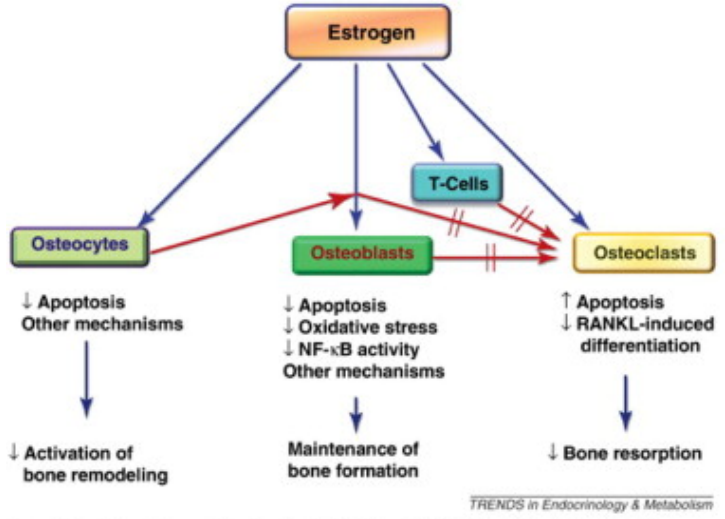
Bone Health and Breast Cancer

- Breast cancer is the most common cancer in women worldwide
- Peak incidence is in postmenopausal age (50-69 y)
- There is a high prevalence of breast cancer long term survivors, thus cancer treatment-induced bone loss (CTIBL) is the most common long term adverse event in hormone receptor positive tumours - osteoporosis and resulting fractures which can impact on QOL and survival
- CTIBL results in a decrease in bone mineral density (BMD)
  - Premature menopause from chemotherapy or use of GnRH agonist
  - Endocrine therapy
  - Compounded by the fact that many women with breast cancer are postmenopausal with an increased risk of bone density loss
- 70-80% of early breast cancer patients will be on adjuvant endocrine therapy for at least 5 years used to improve DFS and OS in hormone receptor + breast cancer

Bone Health and Breast Cancer

- Females reach peak bone mass at the end of skeletal maturation, predicted median age for females in early 30s
  - Genetic factors
  - Physical activity
  - Diet
  - Smoking
  - Alcohol
  - Hormonal status
- After menopause, there is increased bone turnover and accelerated BMD loss and microstructural alteration due to a rapid decline in oestrogen level
  - Oestrogen inhibits osteoclasts and promotes bone densification by stimulating osteoblast osteoprotegerin production which inhibits RANKL binding
  - Annual decrease in BMD of 2% in first 10 years after menopause





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Bone Health and Breast Cancer

- Endocrine therapy
  - Selective oestrogen receptor modulator eg Tamoxifen which in postmenopausal women has a pro-oestrogenic effect on bone and in premenopausal women induces bone loss
  - Aromatase Inhibitors – non steroidal eg anastrozole and letrozole and steroidal eg exemestane which reduces biosynthesis of oestrogens and causes annual BMD loss approx. 2%
- Endocrine therapy is likely to be an aromatase inhibitor (up front or switch)
- Major effect on bone loss appears to be in first 5 years of adjuvant therapy
- Chemotherapy-induced ovarian failure

Bone Health and Breast Cancer

- Assessment of fracture risk
  - DEXA scan at baseline and monitoring during adjuvant therapy (1-2 yearly)
  - Can underestimate the risk for CTIBL and no consensus on T-score threshold for intervention
  - FRAX tool was not designed to evaluate fracture risk in breast cancer women
  - Other tools under investigation – trabecular bone score based on DEXA lumbar spine image, bone biomarkers (eg bone formation: serum bone alk phos, osteocalcin; bone resorption: C-telopeptide, N-telopeptide)
- Breast cancer patients on aromatase inhibitors should have
  - Baseline fracture risk assessment and ongoing monitoring during adjuvant therapy (every 1-2 years)
  - Adequate calcium and vitamin D intake and monitor calcium and Vit D levels

Bone Health and Breast Cancer

- Diet and Lifestyle
  - Adequate calcium (1200 mg) intake
  - Adequate and safe sun exposure
  - Maintain health weight and BMI
  - Stop smoking
  - Avoid excess alcohol consumption <2 standard drinks a day
  - Avoid falls (note treatment-induced peripheral neuropathy)
- Exercise
  - Moderate Resistance and weight bearing exercise – regular, 2-3 days a week
  - Balance training
  - Decreased physical exercise increases the risk

Bone Health and Breast Cancer

- Calcium and Vit D supplementation
  - Recommended if Ca intake <1200 mg/day
  - Ca 1200 mg/day, Vit D 800-1000U/d to achieve 25-OH D levels >50 nmol/L
  - Caution with premenopausal women
- Antiresorptive drugs
  - Bisphosphonates inhibit osteoclast-mediated bone resorption used as a preventative and treatment of bone loss.
    - Used in Australia if >=70 y and T<= -2.5 or if >=50 y and minimal trauma fracture or a high estimated 10 y risk of fracture
    - Three trials have demonstrated upfront bisphosphonate at time of starting AI improved BMD but not fracture risk
    - Zoledronate acid iv 4 mg every 6 months, Alendronate 10 mg o daily, risedronate 5 mg o daily
  - Denosumab (Anti-RANKL antibody which disrupts osteoclast function) - s/c 60 mg every 6 months but has accelerated bone loss on stopping
  - Duration of therapy needs to be individualised based on absolute fracture risk. Most international guidelines recommend administration for the duration of the adjuvant endocrine therapy (ESMO, ASCO)

Bone Health and Breast Cancer – Case 1

- P is a 55 y o post menopausal woman with an early right breast cancer
- 9 mm G2 IC UOQ rt breast, margins clear, 0/3 SLN E+P+H- T1cN0M0
- WLE SLNB
- Adjuvant radiotherapy to right breast
- Commenced on adjuvant endocrine therapy (AI)
- Base line bone density study, no FH of bone health issues or cancer, P is a slim and anxious female, BMI 20

Bone Health and Breast Cancer – Case 1

Site	Baseline	Year 1	Year 2	Year 3	Year 4
Spine	T -1.6	-1.8	-2.2	-2.2	-2.2
Rt femur neck	T -0.9	-1.8	-2.5	-2.6	-2.6
Lt femur neck	T -1.7	-2.3	-2.6	-2.6	-2.5
Rt femur	T -1.6	-1.6	-1.6	-1.9	
Lt femur	T -1.5	-1.7	-2.1	-2.2	
			TBS 1.250	TBS 1.256	
		Arimidex→ Letrozole → Exemestane	Exemestane – pt ceased Vit D levels ok		

Bone Health and Breast Cancer – Case 1

Endocrinologist Plan:

- Dental clearance.
- Vitamin D 1000IU per day.
- Given the Healthy Bones Australia Calcium sheet and suggested P supplement her diet with calcium carbonate 600mg daily.
- Secondary screen including vit D, ALP, Calcium and phosphate, coeliac testing, TFTs,serum EPP, 1mg dexamethasone suppression test, serum tryptase, and a 24 hour urinary calcium collection. Bone turnover markers (CTX, P1NP, ALP) .
- Recommend antiresorptive therapy with Zoledronic acid if continues with AI and consider Zoledronic acid even if not on AI or non pharmacologic measures. Option of Raloxifene discussed

- P opted to remain off AI, did not have any dental work, remains anxious of side effects of antiresorptive meds and of risk of fracture, unable to do effective exercise due to a shoulder injury…

Bone Health and Breast Cancer – Case 2

- K is a 39 y o premenopausal woman with a right breast cancer
- 31 mm G3 IC with DCIS and LVSI+, 1/8 and 0/24 LN with ENE, E+P+H-
- Right mastectomy and SLNB followed by sequential ALND L1-3
- Adjuvant chemo AC x 4 and weekly Paclitaxel x 12
- Adjuvant radiotherapy to right chest wall and SCF/IMC nodes
- Adjuvant AI commenced as menopausal on bloods done post chemo – premature menopause, patient request for BSO
- For baseline bone density study, strong FH of osteoporosis

Bone Health and Breast Cancer – Case 2

Site	Baseline	Year 1
Spine	T -0.5	-0.6
Rt femur neck	T -0.5	-0.4
Lt femur neck	T -0.3	-0.2
Rt femur	T -1.3	-1.1
Lt femur	T -1.2	-1.1
		Arimidex

Bone Health and Breast Cancer – Case 2

- Baseline BMD – osteopaenia
- Baseline Vit D levels low
- On Vit D and Calcium supplements
- On Anastrozole
- Dental review
- Referred to Endocrine Bone Health clinic in view of premature menopause (chemo induced and subsequent risk reduction BSO)

Bone Health and Breast Cancer – Case 2

- Referred to Endocrine Bone Health clinic in view of premature menopause
  - *K has osteopenia by bone densitometry and no history of minimal trauma fracture. She recently commenced aromatase inhibitor therapy in the setting of breast cancer which puts her at risk of ongoing bone loss. Her risk factors for osteoporosis include a more distant family history of osteoporosis, early menopause with the cessation of her menstrual period at least 10 years ago, and vitamin D deficiency. She also likely received dexamethasone during her chemotherapy, which would further contribute to her osteopenia.*
  - *Given that K has multiple risk factors for osteoporosis the most significant of which is her history of premature menopause, it would be reasonable for her to have bisphosphonate therapy for the duration of her aromatase inhibitor therapy. Once she has ceased her aromatase inhibitor, bisphosphonate therapy could be ceased.*
  - *K does not qualify for bisphosphonate therapy on the PBS and so the options would be a private script for weekly Actonel, however I understand that her oncology team may be able to organise bisphosphonate therapy funded via the hospital*
  - *In terms of bone protection, she would only require IV bisphosphonate infusion every 12-18 months, and this could be stretched out further depending on her bone turnover markers. If bisphosphonate therapy were to be given to reduce the risk of bone metastases, I would be guided by oncology as to the preferred treatment intervals.*

Bone Health and Breast Cancer – Case 2

- Referred to Endocrine Bone Health clinic in view of premature menopause

1. *K I have discussed lifestyle factors to improve her bone density including weightbearing and mild-moderate impact exercise. I have suggested that she see her GP for a referral to an exercise physiologist for an exercise program to improve her bone density.*
2. *I have referred K to the Healthy Bones Australia website to self-assess her dietary calcium intake and to see if she can increase this. I have suggested that she reduce her calcium to 600mg per day and if she is able to obtain the other 400mg of calcium through her diet (aiming for 1000mg of calcium per day).*
3. *I have suggested that K start vitamin D 1000IU daily aiming for a vitamin D level of 70-80nmol/L.*
4. *I have asked K to have additional blood tests to exclude other causes of low bone density including coeliac disease.*
5. *I will liaise with K's oncologist as to the possibility of bisphosphonate therapy via their department for the duration of her aromatase inhibitor use, and I have arranged for K to have repeat blood tests for a review in two to four months to discuss the above.*

Bone Health and Breast Cancer – Case 2

- Currently on Anastrozole
- Exercise programme through bone health clinic and is also running
- Continues with Zoledronic acid iv 12 monthly
- Continues Vit D and calcium supplements
- Monitor with BMD and bone turnover markers (CTX, P1NP, ALP) and Calcium, phosphate, Vit D levels

Bone Health and Breast Cancer

- Adjuvant bone modifying agents have been shown to have anti-tumour effect and reduces the risk of bone metastases in post menopausal women and in premenopausal women on ovarian suppression - 14% lower risk of disease recurrence and 3.3% absolute reduction in 10 y mortality in post menopausal women
  - Zoledronic acid iv 4 mg every 3 months for 2 years
  - Zoledronic acid iv 4 mg every 6 months for 3 years
  - Oral bisphosphonates daily for 2-3 years
  - Denosumab not recommended for adjuvant
  - ASCO, ESMO, NCCN guidelines
- Bone is a common site of metastatic disease in breast cancer which can result in bone symptoms (pain, pathological fracture, hypercalcaemia, cord compression) and can contribute to mortality
- Bisphosphonates reduce morbidity from bone metastases by reducing bone related events