Evaluation and Management of Low Bone Density in Premenopausal Women

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- Industry Research Support (To Institution)
  - Eli Lilly
  - Amgen
- Consultancies
  - Radius Pharmaceuticals
- Speakers Bureaus, Financial holdings
  - None
- Discussion of unlabeled use of drugs
  - Teriparatide, denosumab

Key References

1. Cohen A, Shane E. 2013 Evaluation and management of the premenopausal woman with low BMD. Curr Osteoporos Rep 11:276-285.
2. Ferrari S, et al. 2012 Osteoporosis in young adults: pathophysiology, diagnosis, and management. Osteoporos Int 23:2735-2748.
3. Campos-Obando N, et al. 2014 Osteoporotic vertebral fractures during pregnancy: be aware of a potential underlying genetic cause. J Clin Endocrinol Metab 99:1107-1111.
4. Cohen A, et al. 2011 Abnormal bone microarchitecture and evidence of osteoblast dysfunction in premenopausal women with idiopathic osteoporosis. J Clin Endocrinol Metab 96:3095-3105.
5. Choe EY, et al. 2012 Effect of teriparatide on pregnancy and lactation-associated osteoporosis with multiple vertebral fractures. J Bone Miner Metab 30:596-601.
6. Cohen A, et al. 2013 Teriparatide for idiopathic osteoporosis in premenopausal women: a pilot study. J Clin Endocrinol Metab 98:1971-1981.
7. Langdahl BL, et al. 2009 Teriparatide versus alendronate for treating glucocorticoid-induced osteoporosis: an analysis by gender and menopausal status. Osteoporos Int 20:2095-2104.
8. Grossman JM, et al. 2010 American College of Rheumatology 2010 recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Care Res(Hoboken) 62:1515-1526.

Ms. A.A., 29 yo healthy woman

- Fractured left hip after minor fall
- BMD below expected range for age
  - -2.5 at spine, -2.8 at total hip, -3.1 at femoral neck
- Menarche age 15, regular menses, no amenorrhea, G0P0
- PMH unremarkable, no medications, tobacco, ETOH
- + FH osteoporosis - maternal aunt & grandmother
- Physically active, 2 servings dairy/day
- Slim but not undernourished
  - 5'3" (160cm) 100lb (45.4 kg) BMI 17.7 kg/m^2
- No blue sclerae, kyphosis, bone tenderness
- Routine and special labs normal
- Bone turnover markers in normal premenopausal range

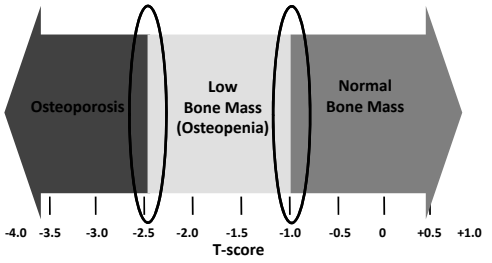
Osteoporosis in Premenopausal Women

- Uncommon
- Most have a secondary cause
- Difficult to diagnose in absence of low trauma fractures

Outline

- Osteoporosis in premenopausal women
  - Diagnosis
  - Etiology
  - Evaluation
- Management of osteoporosis in premenopausal women with
  - Secondary osteoporosis
  - Idiopathic osteoporosis

World Health Organization T Scores



T scores correlate with life time fracture risk for <u>postmenopausal</u> Caucasian women.

Diagnosis of Osteoporosis in **<u>POST</u>**menopausal Women

- Based on the WHO classification [1]
- Areal BMD by DXA
  - T-Score <u>≤</u> -2.5 SD **<u>below young adult mean</u>** at spine, hip or forearm

No comparable data are available for <u>PREmenopausal</u> women.

fractures in **<u>POST</u>**menopausal women

1. WHO Tech Rep Ser 1994;843:1-129
2. Cummings, N Engl J Med. 1995;332:767-73
3. Cooper, Bone. 1993;14 Suppl 1:S89-97
4. Dargent-Molina, Osteoporos Int 2002;13:593-9
5. De Laet, J Bone Miner Res. 1998;13:1587-93

Indications for Treatment of Osteoporosis in **<u>POST</u>**menopausal Women

- Low areal BMD by DXA (T score <u>≤</u> -2.5)
- Low trauma fractures

No clear intervention thresholds for <u>PREmenopausal</u> women.

  - By FRAX

Diagnosis of Osteoporosis in **<u>PRE</u>**menopausal Women is **<u>NOT</u>** Straightforward

Measurement of BMD by DXA has pitfalls in **<u>PRE</u>**menopausal Women

In young women, low areal BMD by DXA may be due to…

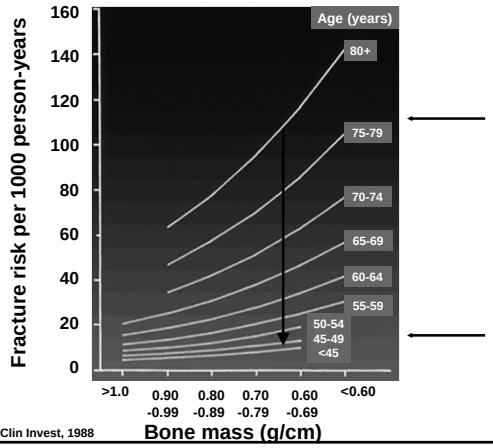
- Low Peak Bone Mass [1-3]
  - Genetics
  - Suboptimal bone mass accrual during adolescence due to lifestyle choices, medical conditions or drug exposures
- Statistical Definition of Z or T Score – in population of normal women
  - 2.5% will have Z score <u>≤</u> -2.0
  - 0.5% will have T score <u>≤</u> -2.5
- Small Stature
  - DXA underestimates BMD in small individuals
- Constitutional Leanness [4-6]
  - Non-pathological state of underweight, normal menses, often familial
  - Low BMD by DXA
  - Abnormal microarchitecture, low strength by HR-pQCT

1. Bonjour et al., Med Sport Sci 2007. 2. Chevalley et al., JCE&M 1998. 3. Ferrari et al., JCE&M 1998.
4. Bossu et al., Am J Physiol Endocrinol Metab 2007 5. Fernandez-Garcia et al., Br J Nutr 2009 6. Galusca et al., JCE&M 2008

Low BMD in <u>YOUNG</u> women is not associated with the same risk of fracture as low BMD in <u>OLDER</u> women.

- Premenopausal women are estrogen replete and have more muscle, lower bone turnover, thicker cortices, better trabecular connectivity and fewer falls
- Incidence and prevalence of fractures **much lower** in **<u>PRE</u>**menopausal than **<u>POST</u>**menopausal women [1-5]
  - Even when BMD is very low

1. Thompson, Injury, 2004 2. Melton, Osteoporos Int, 1998 3. Hosmer, Osteoporos Int, 2002
4. Wu, Arch Intern Med, 2002. 5.Hsu, Am J Clin Nutr, 2006



Hui et al., J Clin Invest, 1988

The 2007 ISCD Guidelines for Reporting BMD Results in **PRE**menopausal Women

Use the Z SCORE, NOT the T SCORE!

Z scores compare people to age-matched controls instead of peak bone mass (age 30)

In premenopausal women and men < age 50

- Z scores above -2.0 should be reported as "within the expected range for age"
- Z scores below -2.0 should be reported as "below the expected range for age"

Goal: Avoid terms like "osteoporosis" and "osteopenia" as their predictive meaning less clear in young women

www.iscd.org

Does not apply to perimenopausal women where the T-score is now used

A premenopausal woman can be considered to have osteoporosis when she has……

- Low BMD - Z-score ≤ -2.0 or T score ≤ -2.5

  +
- Secondary cause of osteoporosis
  - e.g., glucocorticoids, hypogonadism, celiac disease, hyperparathyroidism, rheumatoid arthritis

OR

- History of vertebral or non-vertebral low-trauma fracture(s) at major site
  - Whether or not BMD is frankly low

What about premenopausal women with low BMD (T-score ≤-2.5, Z score ≤-2.0) **BUT NO SECONDARY CAUSE AND NO FRACTURES**?

- Neither ISCD nor IOF would say such a woman has osteoporosis.
- I am not convinced that is true.

Etiology & Evaluation of Premenopausal Osteoporosis

Who Should Be Evaluated?

- Women with fragility fracture(s) or prevalent vertebral fracture(s), regardless of BMD
- Women with low BMD
  - Z score ≤ -2.0
  - T score ≤ -2.5

Goals of Evaluation

- Identify secondary causes of osteoporosis
- Especially treatable causes

Secondary Causes of Osteoporosis in Young Women

- Genetic
  - Idiopathic hypercalciuria
  - Osteogeneis imperfecta
  - Thalassemia
- Endocrine
  - Estrogen deficiency
    - Amenorrhea (except pregnancy)
    - Eating disorders - anorexia, bulemia
    - Prolactinoma, Sheehan's
  - Hyperthyroidism
  - Cushing's syndrome
  - Primary hyperparathyroidism
- Gastrointestinal
  - Celiac disease
  - Malabsorption
  - Inflammatory bowel disease
  - Lactose intolerance
- Rheumatologic
  - Rheumatoid arthritis
  - Systemic lupus erythematosis
- Pulmonary
  - Cystic fibrosis
  - Emphysema
- Medications
  - Prednisone
  - Antiepileptic drugs
  - GnRH agonists
  - Thyroid hormone
  - Depo-Provera
  - Cancer chemotherapy
  - SSRIs
  - PPIs
  - HAART
- Miscellaneous
  - Major depression
  - Pregnancy-associated
  - HIV
- Idiopathic

Most Common Causes of Osteoporosis in Premenopausal Women

- Glucocorticoid excess
- Premenopausal estrogen deficiency
- Eating disorders
- GI disease
  - Celiac disease, inflammatory bowel disease, malabsorption
- Medications
  - Antiepileptic drugs, cancer chemotherapy, prednisone
- Alcoholism
- Primary hyperparathyroidism
- Osteogenesis imperfecta
- **Idiopathic**

Khosla et al, Bone 1994 *Kulak et al, Endocr Pract, 2000* *Bagur et al., ASBMR 2014 SU0312*
Peris et al, Sem Arthr Rheum, 2003 *Cohen et al, J Women's Health, 2009*

Secondary Causes of Osteoporosis in Young Women How often will you find a cause?

- In a population-based study of ♂/♀ age 20-44
  - 90% had a secondary cause [1]
- In series from tertiary referral centers (young ♀)
  - Only ~50% had a secondary cause [2-5]

1. *Khosla et al, Bone 1994* 2. *Kulak et al, Endocr Pract, 2000* 3. *Peris et al, Sem Arthr Rheum, 2003*
2. 4. *Cohen et al, J Women's Health, 2009* 5. *Bagur et al., ASBMR 2014 SU0312*

Evaluation of Low BMD in a Premenopausal Woman

A careful history and physical exam are KEY

Ask about
- Fractures
- Family history of fractures
- Kidney stones
- Menstrual history
- Dieting & exercise behavior
- Eating disorders
- Subtle GI symptoms
- Medications, including OTC supplements

Look for signs of
- Cushing Syndrome
- Thyroid hormone excess
- Systemic mastocytosis – urticaria, dermatographia
- Inflammatory disease
- Connective tissue disorders
  - Osteogenesis imperfecta
  - Ehlers-Danlos

Initial Laboratory Evaluation

- Complete blood count
- Serum calcium, phosphate
- Electrolytes, renal function
- Serum albumin, transaminases, total alk phosphatase
- Serum TSH
- Serum 25-hydroxyvitamin D
- 24 hour urine for calcium, creatinine, free cortisol

Additional Laboratory Tests **As Indicated**

- Estradiol, LH, FSH, prolactin
- PTH
- 1,25-dihydroxvitamin D
- Iron studies
- Vitamin A (retinol)
- Celiac screen
- Serum/urine protein electrophoresis
- Erythrocyte sedimentation rate or C-reactive protein
- Serum tryptase and histamine
- Genetic testing for OI, EDS
- Whole exome sequencing for mutations in Wnt, LRP5/6, other genes?

Bone Turnover Markers??

- If low or normal
  - Suggests prior bone loss or low peak bone mass
- If above premenopausal range
  - Suggests ongoing bone loss
- Cautionary notes:
  - Wide normal range
  - Highly variable
  - Must be interpreted according to age
    - Physiologically high in growing children
    - High after fractures

Tetracyline-labeled Transiliac Bone Biopsy?

- Not widely available
- Primarily a research tool
- May be indicated in patients with idiopathic low-trauma fractures
- May identify other sources of bone fragility and guide therapy
- May be more accurate reflection of bone turnover at the tissue level than bone turnover markers

Idiopathic Osteoporosis (IOP) [1,2]

- Operational definition
  - Premenopausal women and men < 50
  - Otherwise healthy
  - Normal gonadal function
  - No secondary cause of bone loss
- Usually Caucasian
- Often present in mid-30s
  - May present during pregnancy or lactation
- One or more low trauma fractures
  - Cluster over 5-10 yrs
- May be mild or devastating

1. Albright & Reifenstein, 1944
2. Khosla et al, Bone 1994

IOP Without Fractures?

- Clinical significance of isolated low areal BMD in otherwise healthy young woman uncertain
  - Short-term fracture risk increased?
  - Microarchitecture - normal or abnormal?

Do women with Fractures differ from those with Low BMD?

Cross-sectional Case-Control Study

Control – 40

- No adult fractures
- Normal BMD – Z score ≥ -1.0

Fracture group - 45

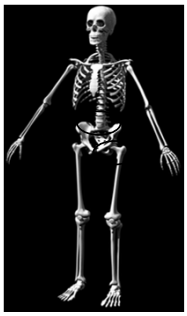
- 1-12 adult fractures
- Mean age at 1st fracture – 30
- Fracture type
  - Vertebrae, ribs, hip, pelvis, forearm, humerus, ankle, metatarsal

Low BMD group - 19

- No low trauma adult fractures

Cohen et al., Osteoporos 2012, 23:171-82

Central QCT of Spine and Hip in IOP



Avoids problem of apparent low areal BMD by DXA in small people

Measures

- Important fracture sites
- Bone size
- Volumetric BMD at the spine and hip
- Cortical thickness at hip

Lang et al JBMR 2004, 2006; Cohen, et al., J Clin Endocrinol Metab 2011

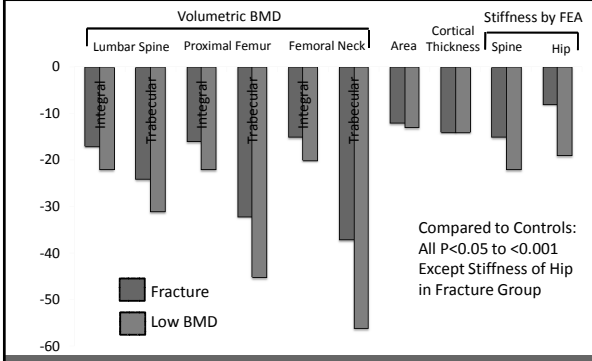
In Premenopausal IOP, Low Areal BMD by DXA (Z ≤-2.0) Predicts Low Volumetric BMD by cQCT

Used cQCT results from Controls to calculate Z-scores for IOP Subjects

- At the spine, 18 of 19 Subjects with Z ≤-2.0 by DXA also had central QCT Z scores ≤-2.0
- Positive predictive value of DXA for cQCT Z-score ≤-2.0
  - 95% at the lumbar spine
  - 90% at the total hip
  - 86% at the femoral neck

Cohen, et al., J Clin Endocrinol Metab 2011

Central QCT in IOP: % Lower Than Controls



Cohen, et al., J Clin Endocrinol Metab 2011

Bone Micro-architectural Deficits

40 Controls **45 Fracture** **19 Low BMD**

3D Imaging:
Central QCT of the spine and hip
Peripheral HR-pQCT of the radius and tibia
Bone biopsies at the iliac crest

Cortical Bone:
↓ Density, ↓ Thickness
↑ Porosity
Trabecular Bone:
↓ Density
↓ Tb Number
↑ Tb Separation
↓ Stiffness

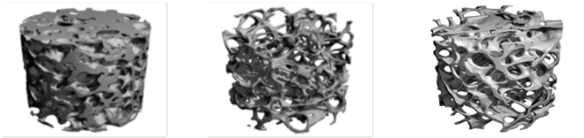
Control Fracture Low BMD

Cohen et al, JCEM 2009

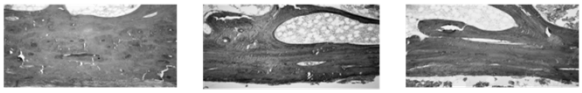
Bone Micro-architectural Deficits on Transiliac Biopsy

40 Controls **45 Fracture** **19 Low BMD**

Trabecular Bone Microstructure by MicroCT



Cortical Thickness and Porosity by 2D Histomorphometry



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Cortical Bone:
↓ Density, ↓ Thickness
↑ Porosity
Trabecular Bone:
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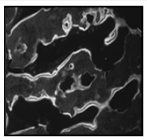
↓ Tb Number
↑ Tb Separation
↓ Stiffness

Comparable deficits in women with fractures and those with only Low BMD

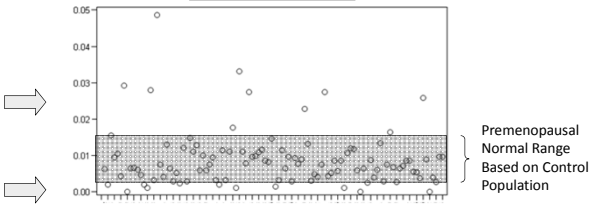
Cohen et al, JCEM 2009 Cohen et al, JCEM 2011 Cohen et al, JCEM 2012

Remodeling Was Heterogeneous



- No significant group differences between Controls and Fracture or Low BMD
- High, normal and low turnover (BFR/BS)

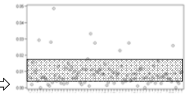
Bone Formation Rate

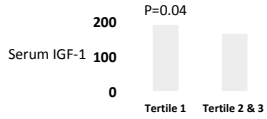


Cohen et al., JCE&M 96:3095-3105, 2011

Women in **LOWEST** Tertile of BFR

- Lowest serum bone turnover markers
- Lowest volumetric BMD & strength
- Significantly **HIGHER** serum IGF-1
- c/w IGF-1 resistance at the osteoblast level?

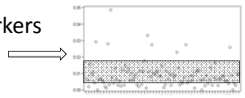




Cohen et al., JCE&M 96:3095-3105, 2011

Women in **HIGHEST** Tertile of BFR

- Highest serum bone turnover markers
- Higher $1,25(OH)_2D$
- Higher Urine Calcium and PTH
- c/w Idiopathic Hypercalciuria?



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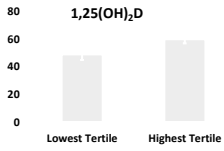
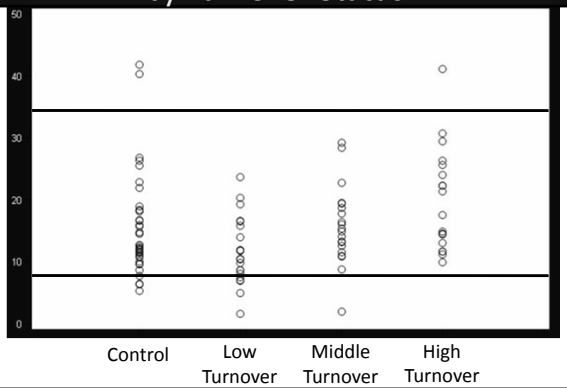


Cohen et al., JCE&M 96:3095-3105, 2011

Did serum bone turnover markers predict bone formation rate on iliac crest bone biopsies in women with IOP?

NO

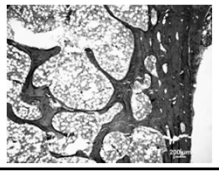
Serum Osteocalcin in Premenopausal IOP by Turnover Status



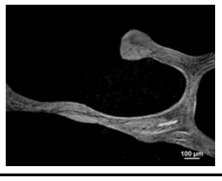
Ms. A.A. Tetracycline-Labeled Transiliac Biopsy

- Thin, porous cortices
- Thin, disconnected trabeculae
- Normal eroded surface
- Normal mineralization rate, no osteomalacia
- Low bone formation rate, DESPITE normal bone turnover markers

Bone Volume Fraction 19.8%
Cortical Width 661 microns



Bone Formation Rate 0.006 mm2mm/yr



IOP in Premenopausal Women

- Consistent deficits in volumetric BMD, microarchitecture, stiffness at spine & hip [1], distal radius & tibia [2], iliac crest [3]
- Heterogeneous turnover - varying pathogeneses [4,5]
  - Primary osteoblast dysfunction, IGF-1 resistance
  - Idiopathic hypercalciuria

1. Cohen et al., JCE&M 97;4244–4252, 2012
2. Cohen et al., JCE&M 94;4351-4360, 2009
3. Cohen et al., JCE&M 96;3095-3105, 2011
4. Cohen et al., Osteoporos 23; 171-82, 2012

Conclusions

- Assessment of bone turnover by bone biopsy may provide clues to pathogenesis of IOP in individual patient

Fracture and Low BMD subjects:
Differed comparably from Controls
Did NOT differ from each other
Selection bias?
Part of a continuum?
Fractures due to happenstance?

Outline

- Osteoporosis in premenopausal women
  - Diagnosis
  - Etiology
  - Evaluation
- Management of osteoporosis in premenopausal women with
  - Secondary osteoporosis
  - Idiopathic osteoporosis

The challenge for physicians caring for premenopausal women with osteoporosis

1. To decide WHETHER to treat
2. To decide HOW to treat

Management of Premenopausal Osteoporosis

- General Measures
  - Adequate nutrition, calcium, vitamin D, exercise
  - Avoid tobacco, excess alcohol

  Makes sense but minimal effects on BMD [1]
- Specific therapy of secondary cause(s) often yields large increases in BMD
  - Celiac Disease [2-5], Primary hyperparathyroidism [6]
  - Control inflammation in chronic inflammatory states (RA[7], inflammatory bowel disease [8,9])

1. Peris, Clin Rheumatol, 2006 2. Sategna-Guidetti, Aliment Pharmacol Ther. 2000 3. Ciacci, Am J Gastroe***nterol.*** 1997
4. McFarlane, Gut, 1996 5. Mautalen, Am J Gastroenterol. 1997 6. Lumachi, Ann N Y Acad Sci. 2007

Conservative Treatment in Premenopausal Women With Unexplained Fractures

- 16 women
- Calcium, vitamin D and exercise
- BMD followed annually for average of 3 yrs
  - Spine BMD increased by ~2%
  - Femoral neck BMD increased by ~6%
- **NO** new fractures

Peris, Clin Rheumatol, epub August, 2006

Ms. A.A.
Conservative Management

- Calcium intake 1200 mg day from food and supplements
- Vitamin D ~1000 IU daily
- OCP for birth control
- Over next 10 years
  - BMD remained very low but quite stable
  - 2 pregnancies with expected bone loss
  - No new fractures
- Subsequent evaluations for 2^{o} osteoporosis
  - No new medical diagnoses or medications

Management of Premenopausal Osteoporosis

- Pharmacologic therapy **rarely justified** unless
  - Fractures
  - Ongoing bone loss with conservative Rx
  - Extremely low BMD (T or Z score ≤-3.0)

Management of Premenopausal Osteoporosis

- If drug therapy necessary, avoid SERMs (e.g., raloxifene)
  - Cause bone loss in premenopausal women [1,2]
- Use bisphosphonates with caution in childbearing women [3]
  - Long residence in the skeleton and cross placenta
  - Animal studies - adverse effects on fetus (high doses)
  - Case reports suggest safe in pregnancy & lactation [4-9]
- Teriparatide & Denosumab contraindicated in pregnancy

1. Powles, J Clin Oncol, 1996 2. Vehmanen, J Clin Oncol, 2006 3. Stathopoulos, Hormones (Athens) 2011
4. Biswas, Osteoporos Int, 2003 5. Chan, JCE&M 2006 6. Djokanovic, J Obstet Gynaecol Can 2008
7. Illidge, Clin Oncol (R Coll Radiol) 1996 8. Munns J Bone Miner Res 2004 9. O'Sullivan Osteoporos Int 2006

BPs or Teriparatide Improve BMD in Premenopausal Women With Secondary Osteoporosis

- Anorexia nervosa
- Chemotherapy induced amenorrhea
- GnRH therapy for endometriosis
- Crohn's disease (+ infliximab)
- Cystic fibrosis
- Thalassemia major
- HIV-associated osteopenia
- Glucocorticoid-induced osteoporosis

CAVEATS

1. BPs and TPTD are only FDA-approved in premenopausal women taking Glucocorticoids.
1. No data that treatment with BPs or TPTD prevent fractures in premenopausal women.

Ferrari et al., Osteoporos Int. 2012; 23:2735-2748

Glucocorticoids in Premenopausal Women

- Bisphosphonates and teriparatide prevent bone loss and/or increase BMD in premenopausal women on GCs [1-4]

HOWEVER

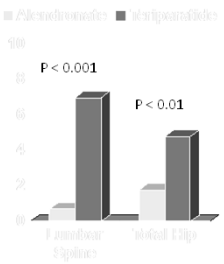
- Premenopausal women on GCs may not lose bone
- Bone loss more likely if oligomenorrhea or amenorrhea
- Less likely to fracture on GCs than postmenopausal women

1. Nakayamada, J Rheumatol, 2004
2. Sato, J Rheumatol, 2003
3. Nzeusseu, Lupus, 2005
4. Roux, Osteoporosis Int, 2011

Teriparatide vs Alendronate for Treatment of GC-Induced Osteoporosis

Saag et al, NEJM, 2007

- Randomized active comparator trial of 528 patients with GIOP
- Sub-analysis of BMD changes and fractures in 51 premenopausal women
- No fractures in either group



Langdahl et al. Osteoporos Int, 2009;20:2095-04

Recommendations For Premenopausal Women on GCs: ACR 2010

- Assess for
  - prevalent fragility fractures
  - childbearing potential
  - dose and likely duration of GC therapy
- Measure BMD
- Prescribe calcium and vitamin D
- Prescribe estrogen if deficient

American College of Rheumatology. *Arthritis Care and Research 62;1515-26, 2010*

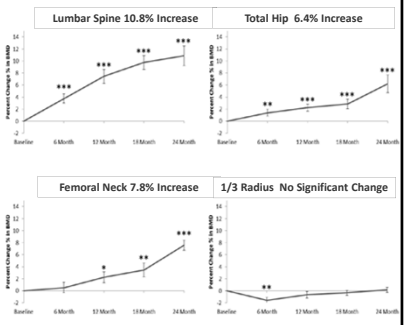
Recommendations For Premenopausal Women on GCs: ACR 2010

- In women of NONchildbearing potential, prescribe BPs if
  - Prevalent fragility fracture(s)
  - Prednisone ≥ 5 mg/day for ≥ 1 month
- In women of childbearing potential, prescribe BPs if
  - Prevalent fragility fracture(s)
  - Prednisone ≥ 7.5 mg/day for ≥ 3 months
- No consensus about
  - Those with no prevalent fragility fracture
  - Women of childbearing potential with prevalent fracture on GCs for < 3 months

American College of Rheumatology. *Arthritis Care and Research 62;1515-26, 2010*

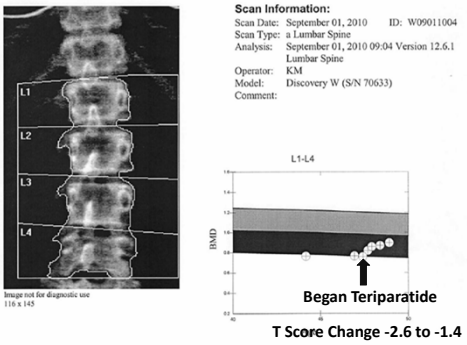
Teriparatide for Premenopausal IOP: Open-Label Observational Study

- 21 women
- Mean age 39
- TPTD 20 mcg x 2 yrs
- BMD every 6M
  - % change from baseline
- Transiliac biopsies
  - Baseline and 18M
- HR-pQCT
  - Baseline and 18M

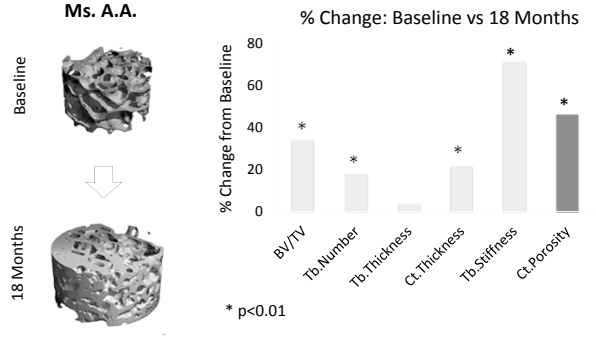


Cohen A et al. J Clin Endocrinol Metab 2013

Ms. A.A. Spine BMD Changes on Teriparatide



Teriparatide for Premenopausal IOP: Bone Structural Changes on Biopsies



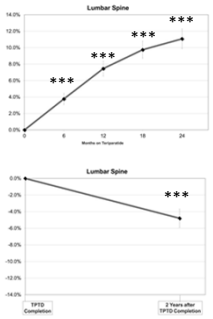
Cohen A et al. J Clin Endocrinol Metab 2013

What about after TPTD?

- In postmenopausal women and men, BMD declines after TPTD stopped if not followed by anti-resorptive therapy.

In menstruating women, is endogenous estrogen production sufficient to prevent this?

Partial Loss at Lumbar Spine 2 Years after Stopping TPTD



- 15 women from pilot study rescanned at ~ 2 yrs
- ~5% loss at spine (p<0.001)
- Stable BMD at total hip and femoral neck
- Those who lost >3% BMD at spine were older
  - 46 vs 38; p=0.046

Cohen A et al. ASBMR 2014; Poster SUO0373

Do premenopausal women need antiresorptive treatment to prevent bone loss after teriparatide?

PROBABLY

Which antiresorptive should be used?

DEPENDS ON THE CLINICAL SITUATION

Estrogen?

Bisphosphonates?

Denosumab?

Possible future choices – more anabolic therapy?

Anti-Sclerostin Antibodies?

PTHrP analogues?

Key Diagnostic Points

- Diagnosis of osteoporosis in premenopausal women most secure if secondary cause or low trauma fractures
- Low areal BMD by DXA in otherwise healthy women should be interpreted with caution
  - **But may reflect low volumetric BMD and strength**
- Bone turnover markers of limited assistance in assessing bone turnover
  - Bone biopsies may be helpful

Key Management Points

- Crucial to assess for secondary causes of bone loss and treat specifically

No fracture data are available for treatment studies of premenopausal women…

Given relatively low fracture rates in premenopausal women, there probably never will be…

premenopausal women with various causes of bone loss

FDA-Funded RCT of TPTD in Premenopausal IOP

- New study enrolling
- Randomized, placebo-controlled, single switch-over
- Quadruple tetracycline-labeled transiliac biopsy at 3 months
- Funded by FDA Orphan Products/Disease Branch
- At completion, observation vs antiresorptive Rx with denosumab funded by Amgen and hopefully FDA
- To refer women with IOP:
  - Call 212-305-7225

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Thank you!