Osteoporosis and DXA Overview

Neil Binkley, MD

November 2, 2006
Osteoporosis: A systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, resulting in increased bone fragility and susceptibility to fracture.

More Recent NIH Consensus Definition Includes “Bone Quality”

• Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture

• Bone strength reflects two main features:
  • bone density
  • bone quality
Osteoporosis is Usually Multifactorial

- Low bone mass at skeletal maturity (~ age 30)
- Advanced age
- Low calcium and/or vitamin D intake
- Use of prednisone (corticosteroids)
- Smoking/High alcohol consumption
- Lower body weight
- Low physical activity
- Loss of estrogen/testosterone
Bone Density Declines with Advancing Age

This decline leads to increased risk for osteoporotic fracture, most commonly of the spine/hip/wrist.
Men

Hip fracture risk in men reaches the same level as in women, but at an age ~6 years older.

With Bone Loss, Fracture Risk Increases in Both Men and Women

Hip fracture risk in men reaches the same level as in women, but at an age ~6 years older.

Cooper, JBMR 1992
Of the 6 million fractures per year in the US, approximately 1.5 million are due to osteoporosis.

- Hip: 700,000
- Wrist: 250,000
- Other: 300,000

Only ~25%-30% of morphometric vertebral fractures are diagnosed clinically.
Consequences of Osteoporotic Fracture

- Pain; acute and/or chronic
- Reduced ability to perform activities of daily living
  - ~50% of people able to live independently after a hip fracture
- Change in body habitus
- Respiratory compromise
- Depression/anxiety/fear of falling
- Cost ~$13 billion annually
- Death; ~20% one year mortality following hip fracture
Survival Rates After Fractures

Survival
Time after fracture (years)

Expected
Observed

% Survival

Hip Fracture
(relative survival = 0.82)

Vertebral Fracture
(relative survival = 0.81)

How Common is Osteoporosis?

Women  ~50%

Men  ~33%
What Does Someone with Osteoporosis Look Like?
Osteoporosis is Not Simply “Getting Old”
Think of Osteoporosis in the Same Way That You For High BP or High Cholesterol

<table>
<thead>
<tr>
<th>Disease</th>
<th>Clinical measure</th>
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<tbody>
<tr>
<td>Hypertension</td>
<td>BP</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Lipids</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>BMD</td>
</tr>
</tbody>
</table>

Outcome

CVA
MI
FX
How Do You Know if Your Patient Has High Cholesterol?

Measure it!
How Do You Know if Your Patient Has Low Bone Density?

* MEASURE IT!
* Risk factors do not work to guess bone density
  * Advanced age
  * Female gender
  * Caucasian race
  * Thin
  * Family history of osteoporosis
  * Etc, etc.
Risk Factors Do Not Allow Prediction of BMD

IMPACT Trial: ~7000 postmenopausal women had BMD measurement and risk factor assessment

48% of those with osteoporosis had no risk factors

53% of those with risk factors did not have osteoporosis

Watts, Arth Rheum 2001
“You can’t find a fever if you don’t check the temperature.”

G. Magnin, M.D.
Radiation Exposure

- DXA (spine & hip) ~2-3 uSv
- PA CXR ~50 uSv
- L spine radiograph ~550 uSv
- Abd CT scan ~4000 uSv
- Natural background ~6-8 uSv/day
ISCD Indications for BMD Testing

- All women aged 65 and older
- Postmenopausal women under age 65 with risk factors
- All men aged 70 and older
- **Adults with a fragility fracture**
- Adults with a disease or condition associated with low bone mass or bone loss
- Adults taking medications associated with low bone mass or bone loss
- Anyone being considered for pharmacologic therapy
- Anyone being treated, to monitor treatment effect
- Any not receiving therapy in whom evidence of bone loss would lead to treatment
## Indications for BMD Testing

<table>
<thead>
<tr>
<th>Category</th>
<th>USPSTF</th>
<th>NOF</th>
<th>AACE</th>
<th>ACR</th>
<th>ACOG</th>
<th>OSC</th>
<th>ISCD</th>
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<td>✔</td>
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<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>

- Risk factors vary according to organization
- Some organizations only consider postmenopausal women

Bray, www.iscd.org
Fracture Risk Increases With Age

But BMD Measurement Declines

Fracture Risk Increases With Age

But BMD Measurement Declines

Cooper JBMR, 1992

Neuner, JAGS 2006
Average Life Expectancy; 2001 US
Female 79.5 years, Male 74.1 years

CDC/Natl Center for Health Statistics
www.cdc.gov/nchs/fastats/lifeexpec.htm
“Bone mineral density measurement should be obtained routinely in all women over the age of 65 years and in men and younger women who have had a fragility fracture. Compliance with this recommendation alone would be a great advance in comparison with current practice.”

Raisz, NEJM 2005
BMD Measurement is Not Being Done Following Fracture

Retrospective cohort study NW US HMO; 1171 men Age > 65 years with any new fracture

Feldstein, Osteoporos Int, 2005
BMD Measurement Needs to Become More “User Friendly”
Densitometers Measure BMD

But T-scores Are Used For Diagnosis
WHO Diagnostic Categories

These Criteria Apply ONLY to the L-spine, Proximal Femur and 1/3 Radius

Normal

Osteopenia

-1.0

Osteoporosis

-2.5

Severe Osteoporosis

WHO Technical Series, 1994
T-score Compares With Young Adult;  
Z-score with Age-Matched

\[ T\text{-score} = \frac{\text{Patients BMD} - \text{Young Normal Mean BMD}}{\text{SD of Young Normal}} \]

\[ Z\text{-score} = \frac{\text{Patients BMD} - \text{Age Matched Mean BMD}}{\text{SD of Age Matched}} \]
T-score Calculation Example

- **ASSUME**
  - Mean YN BMD = 1.200 g/cm²
  - SD of the YN population = 0.100 g/cm²
  - Your patient’s BMD is 1.000 g/cm²

\[
1.000 - 1.200 = -0.200 \\
-0.200/0.100 = -2.0
\]
Why Use T-scores?

▫ BMD is not measured the same using different densitometers

▫ There are differences in
  • Technologies of x-ray generation
  • Edge detection approaches
  • Region of interest placement

▫ Hologic BMD in g/cm² ~10% lower than GE Lunar

▫ **T-scores allow use of same diagnostic criteria with instruments of different manufacturers**
T-Score Used for Diagnosis

Z-Score Used for Children and Health Adults Under Age 50

Clinical Lore that a Z-score of $\leq -2.0$ Indicates Need to Perform Evaluation for Secondary Causes of Bone Loss
Spine and Hip DXA Are the Gold Standard
Apply the WHO Criteria for Diagnosis Using the Lowest T-score of the L1-4 Spine, Total Femur or Femur Neck

Report an Overall Diagnosis, Not Site-Specific Diagnoses
Diagnosis Using WHO: Use the Lowest T-score

Don’t Be Bothered by T-score Discordance

- Ideally, BMD measurement at all sites would yield the same T-score
- That this does NOT occur is referred to as skeletal discordance
Discordance Due to Spine DJD

L1-L4 BMD = 1.248 g/cm²  
T-score = 0.6

Total hip BMD = 0.725 g/cm²  
T-score = -2.3
Use the L1-L4 T-score, However

Exclude vertebrae from analysis if there is a > 1.0 T-score difference between adjacent vertebral bodies.

L1 -3
L2 -2.3
L3  2.4
L4  2.0
L1-2 T-score -2.5
L1-4 -0.5
Need to Use at Least Two Vertebrae
Don’t “Cherry-pick” the Lowest Vertebral Body
When the Spine BMD is Worthless, Measure the Forearm

L1-L4 T-score = 3.2

.3 T-score = -2.9
When Should the Forearm be Measured?
When Hip and/or Spine Cannot be Accurately Measured

- Extensive spinal instrumentation
- Severe scoliosis
- Severe degenerative changes
- Multiple compression fractures
- Bilateral hip replacements
- Obesity (most tables have 300# weight limit)
Isn’t the Forearm a “Peripheral” Site?

“Osteoporosis is defined as a bone mass more than 2.5 SD below the young adult reference mean at the spine, hip or mid-radius.”
The WHO Criteria Apply to the Femur Neck and Total Proximal Femur
Not Ward’s Area or the Greater Trochanter

“This patient has osteoporosis and given her young age should receive teriparatide.”
It is Impossible to Tell if a Person has “Lost” Bone Based on a Single Measurement

HALF OF US ARE BELOW AVERAGE

Don’t tell patients that their BMD is XX% of young normal or that their bones are 95 years old (unless the patient is 95)
"I’m only 51 years old and perimenopausal but I’ve already lost 17% of my bone and have osteopenia."

<table>
<thead>
<tr>
<th>Region</th>
<th>BMD $^1$ g/cm$^2$</th>
<th>Young $^2$ %</th>
<th>Adult $^2$ T</th>
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<tbody>
<tr>
<td>L1</td>
<td>0.923</td>
<td>82</td>
<td>-1.7</td>
</tr>
<tr>
<td>L2</td>
<td>0.972</td>
<td>81</td>
<td>-1.9</td>
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<tr>
<td>L3</td>
<td>1.003</td>
<td>84</td>
<td>-1.6</td>
</tr>
<tr>
<td>L4</td>
<td>0.995</td>
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<td>L1-L2</td>
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<tr>
<td>L1-L3</td>
<td>0.968</td>
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<td>-1.7</td>
</tr>
<tr>
<td>L1-L4</td>
<td>0.975</td>
<td>83</td>
<td>-1.7</td>
</tr>
</tbody>
</table>

$^1$ Bone mineral density
$^2$ Normalized to young adult or average adult
“Shortopenia” is Not a Disease!
Low DXA-measured BMD is Consistent With Osteoporosis

59 year old man with osteoporosis
Hmmm.
59 Year-old Man with “Osteoporosis”

- Status post bariatric surgery
  - weight decrease ~125 pounds
- Back injury while golfing – imaging negative for fracture but noted radiographic osteopenia
- Normal testosterone, thyroid studies
- Calcium: 8.3 mg/dl (8.5-10.4)
- iPTH: 304 pg/ml (7-53)
- 24 hour urine calcium 25 mg
- 25-OH vitamin D 7 ng/ml
Vitamin D Deficiency
Osteomalacia
When Should Follow-up DXA be Performed?

- “It depends”
- Not more frequently than yearly
- Initiation of steroids is an exception (6 months)
- ISCD position; measure one year after initiation of Rx to document response (stability or increase)
- Medicare has defined monitoring interval as no more frequently than every 23 months
Stable BMD on Treatment is Success
12 mo BMD change in ~3000 ALN treated patients

Hochberg, Arthritis Rheum 1999
This is Due to Anti-resorptive Induced Reduction in “Stress Risers”
What is a Real Change on Follow-up DXA?

- Necessary to perform an *in-vivo* precision assessment
  - This is facility, technician and patient population dependent
- At UW, the L1-L4 spine LSC is **0.040 grams/cm²** and **0.020 grams/cm²** at the mean total femur
  - These values will vary between facilities and technologists
  - For example, the L1-L4 LSC at the Wm. S. Middleton VAMC is **0.049 grams/cm²**
- A “decrease” from .890 to .875 g/cm² is no change
Use the BMD in grams/cm$^2$

NOT the T-score When Performing Follow-up DXA

Know What Constitutes a Real Change in BMD at Your Facility

Need to Know Your LSC

If a Precision Assessment Has Not Been Done, Monitoring BMD is Not Possible
“I’m on Drug X but my bone density is going down. Is there anything else that can be done?”

A 0.020 g/cm\(^2\) “difference” is not a real change

12/11/04  
L1-L4 BMD = .705 g/cm\(^2\)  
\(\theta\) T-score = -3.9

1/19/06  
L1-L4 BMD = .685 g/cm\(^2\)  
T-score = -4.1
Precision and Accuracy

- Precision = agreement of serial measurements of the same thing
- Accuracy = ability to determine the “true” value
Use the excel-based precision calculator at iscd.org
If Huge Change in BMD (~10%) Look For Technical Problems
Make Sure You Are Comparing Apples With Apples
8% Decline in BMD on Bisphosphonate Rx

Baseline

Follow-up

L1-L4 BMD 0.717 g/cm²

L1-L4 BMD 0.629 g/cm²
BMD Comparison Between Facilities

- It is not possible to quantitatively compare BMD or to calculate a least significant change between facilities without cross-calibration

Binkley, et. al., J Clin Densitom, 2006
Things NOT To Tell Your Patients About Their DXA

- “Bone loss” without knowledge of prior bone density
- “Mild,” “moderate,” or “marked” osteopenia or osteoporosis
- Separate diagnoses for different regions (e.g., osteopenia at the hip and osteoporosis at the spine)
- Expressions such as “You have the bones of an 80-year-old,” if the patient is not 80 years old
- The change in BMD if it is not a significant change based on the precision error and LSC

Binkley, et. al., J Clin Densitom, 2006
Densitometric Vertebral Fracture Assessment (VFA) is Now Available
VFA is a Quick, Convenient, Low Radiation Tool to Detect Individuals with Unappreciated Vertebral Fractures
Only ~25% of Vertebral Fractures are Clinically Apparent

May be Asymptomatic

...... or Unrecognized

Estimated that ~1% of Back Pain Episodes are Caused by Vertebral Fracture
Moderate and Severe Fractures are Easy to Identify
Indications for VFA

When BMD measurement is indicated, performance of VFA should be considered in clinical situations that may be associated with vertebral fractures.

Examples include:

- Documented height loss of greater than 2 cm (0.75 in) or historical height loss greater than 4 cm (1.5 in) since young adult
- History of fracture after age 50
- Commitment to long-term oral or parenteral glucocorticoid therapy
- History and/or findings suggestive of vertebral fracture not documented by prior radiologic study

Binkley, et. al, JCD, 2006
Why Should We Care About Unappreciated Vertebral Fracture?
Because They Identify People at Higher Risk

Fracture presence and severity predicts future risk.

Fracture Severity at Baseline

% with 1 or more new fractures

- None: 4%
- Mild: 11%
- Moderate: 24%
- Severe: 38%

Because They Identify People at Higher Risk
Absolute Fracture Risk is Coming

A WHO Absolute Fracture Risk (Fracture Probability) Technical Document Will be Published Soon
Relative Risk Does Not Clearly Define Fracture Risk

“Your T-score is -2.0. You are at a four-fold increased risk for fracture.”

Absolute fracture risk in the next 10 years
If femur neck T-score = -2.0

50 year old: 9.2%
80 year old: 20.5%
Numerically More Fractures Occur in People Without Osteoporosis

Only 44% of women and 21% of men who sustain non-vertebral fractures have osteoporosis by BMD

5794 participants in the Rotterdam study; Mean follow-up 6.8 yrs

FN BMD at baseline

<table>
<thead>
<tr>
<th>Condition</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>449</td>
<td>145</td>
</tr>
<tr>
<td>Osteopenia</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

BMD Measurement Identifies Those at High Fracture Risk, But Alone, it is Not Sensitive Enough

By Basing Treatment Decisions Solely on T-score, We Are Missing About Half of Women Who Are At Risk for Fracture
The WHO Paradigm Will Add Clinical Factors to BMD

Fracture Risk

High  Bone Mineral Density  Low

Age 50
Age 65
Age 80

Notably age

Kanis, IOF 2006
And Prior Fracture

Fracture Severity at Baseline

- None: 4%
- Mild: 11%
- Moderate: 24%
- Severe: 38%
Clinical Factors The WHO Will Use to Estimate Fracture Risk

- Age
- BMD
- Prior Fracture
- Ever use of glucocorticoids
- Family history
- Smoking
- Alcohol

Kanis, IOF 2006
Expect the WHO Absolute Risk Approach to Become Part of the DXA Printout

“Based upon age, femur neck BMD and prior fracture, this person’s 10-year risk of hip fracture is 8% and of any fracture is 15%.

Per the National Osteoporosis Foundation, pharmacologic treatment is recommended when the 10-year fracture risk is above xx%.”
What About “Peripheral” BMD Measurements?

- Use of WHO criteria for the diagnosis of normal, osteopenic or osteoporotic BMD inappropriate
- Currently, if central DXA available; don’t make dx of osteoporosis based on peripheral measurement
- Cannot be used to monitor osteoporosis therapy
Conclusion: Application of a single T-score criteria (WHO) is not appropriate for different sites and technologies.
Can/Should the WHO Criteria Be Applied to Populations Other than Postmenopausal Caucasian Women?
A 36 year old healthy woman with a strong family history of osteoporosis has a heel scan done at a health fair and is told that she has “osteopenia.” She has a spine/hip DXA performed. Is this wise? Her spine and hip T-scores are -2.0. What do you tell her?
WHO Criteria Should Not be Applied to Healthy Premenopausal Women

- Z-scores rather than T-scores should be used
- Osteoporosis may be diagnosed if there is low BMD with secondary causes (glucocorticoid therapy, hypogonadism, hyperparathyroidism, etc) or with risk factors for fracture
- The diagnosis of osteoporosis in premenopausal women should not be made on densitometric criteria alone
Osteoporosis: A systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone, with a consequent susceptibility to fracture.
The WHO Criteria Do Not Apply to Young Adults or Children

- Z-scores, not T-scores, are preferred
- This is particularly important in children
- A Z-score of -2.0 or lower is defined as “below the expected range for age” and a Z-score above -2.0 is “within the expected range for age”
A 16 Year-Old Healthy Girl is Referred with “Osteoporosis.” She Was Training for Cross-country and Sustained a Tibial Stress-Fracture While Running. Her Spine T-score is -2.0 and She Has Been Started on Alendronate.
Densitometric Diagnosis In Children

- T-scores should not be used in children
- Z-scores should be used instead
- Spine and total body are the preferred sites to measure
- The diagnosis of osteoporosis in children should not be made on the basis of densitometric criteria alone
- Terminology such as “low bone density for chronologic age” may be used if the Z-score is $<-2.0$
How Should Osteoporosis Be Diagnosed In Non-Caucasians?
The “Correct” Approach to T-score Race-Adjustment is Controversial and Politically Charged. Even the Definition of “Race” is Not Easy
ISCD Position Regarding Osteoporosis Diagnosis in Non-Caucasians

Utilize a uniform Caucasian (universal) normative database and a T-score of -2.5 for osteoporosis diagnosis
Estimated Male Lifetime Fracture Risk

• Age 50, Rochester; 13% Melton JBMR, 1992
• Age 50, Malmo; 22% Kanis Ost Int, 2000
• Age 60, Dubbo; 25% Nguyen Am J Epidemiol, 1996
• Age 50, Dubbo; 32% Nguyen, ASBMR 2005
In men age age 50 and older, T-scores should be used and osteoporosis diagnosed if the T-score is $\leq -2.5$.

The diagnosis of osteoporosis in healthy men under age 50 should not be made on the basis of densitometric criteria alone.
Which Men Should Have Bone Mass Measurement?

WHO task-force (Genant, OI 1999) and ISCD

- Radiographic osteopenia and/or vertebral deformity
- Loss of height or thoracic kyphosis
- Prior low trauma fracture
- Conditions recognized to ↑ risk for bone loss and Fx
  - Hypogonadism/prostate Ca, glucocorticoid rx, hyperparathyroidism, etc

- Screening at age 70
BMD measurement with central DXA at age is recommended [Grade A]

Measuring bone density in men and women after the age of 65 is justifiable
In Some Studies, Spine BMD is Not Lower in Older Men

Melton, JBMR 1998
What Skeletal Sites to Measure in Men?

596 men, clinical DXA scans, age 23-95, mean 65

If “routine” is spine & hip miss 17%

Vallarta-Ast, JCD 2002
Patients With Osteoporotic Fractures Are Not Being Treated

- Panneman MJM et al. Osteoporos Int. 2004
- Jachna CM et al. Osteoporos Int. 2003
- Port L, et al. Osteoporos Int. 2003
- Liel Y et al. Osteoporos Int. 2003
- Cuddihy MT et al. Arch Intern Med. 2002

Retrospective cohort study
NW US HMO; 1171 men > 65 years with any new fracture
Feldstein, Osteoporos Int, 2005
Osteoporosis Screening
Time to Take Responsibility

“The responsibility to ensure appropriate osteoporosis screening and treatment begins with any clinician... The status quo of “missed opportunities” is unacceptable. The buck stops with us.”

Mazanec, Arch Intern Med May, 200
Osteoporotic Fractures Should be Thought of as “Bone Attacks”