



Diagnosis of osteoporosis in CKD patients

Mozhdeh Zabihiyeganeh, M.D.

Associate Professor of Rheumatology

Iran University of Medical Sciences

Osteoporosis definition

- Osteoporosis is a common disease that is characterized by low bone mass with microarchitectural disruption and skeletal fragility, resulting in an increased risk of fracture

Fracture Epidemiology in CKD

- CKD is associated with an increased risk of fragility (low trauma) fractures.
- In addition, the risk of fracture-related mortality increases with the severity of CKD.

Fracture Epidemiology in CKD and ESKD

- The incidence and prevalence of fractures increases with CKD stage and has been reported to be 2- to 17-fold higher in CKD patients compared with the general population.

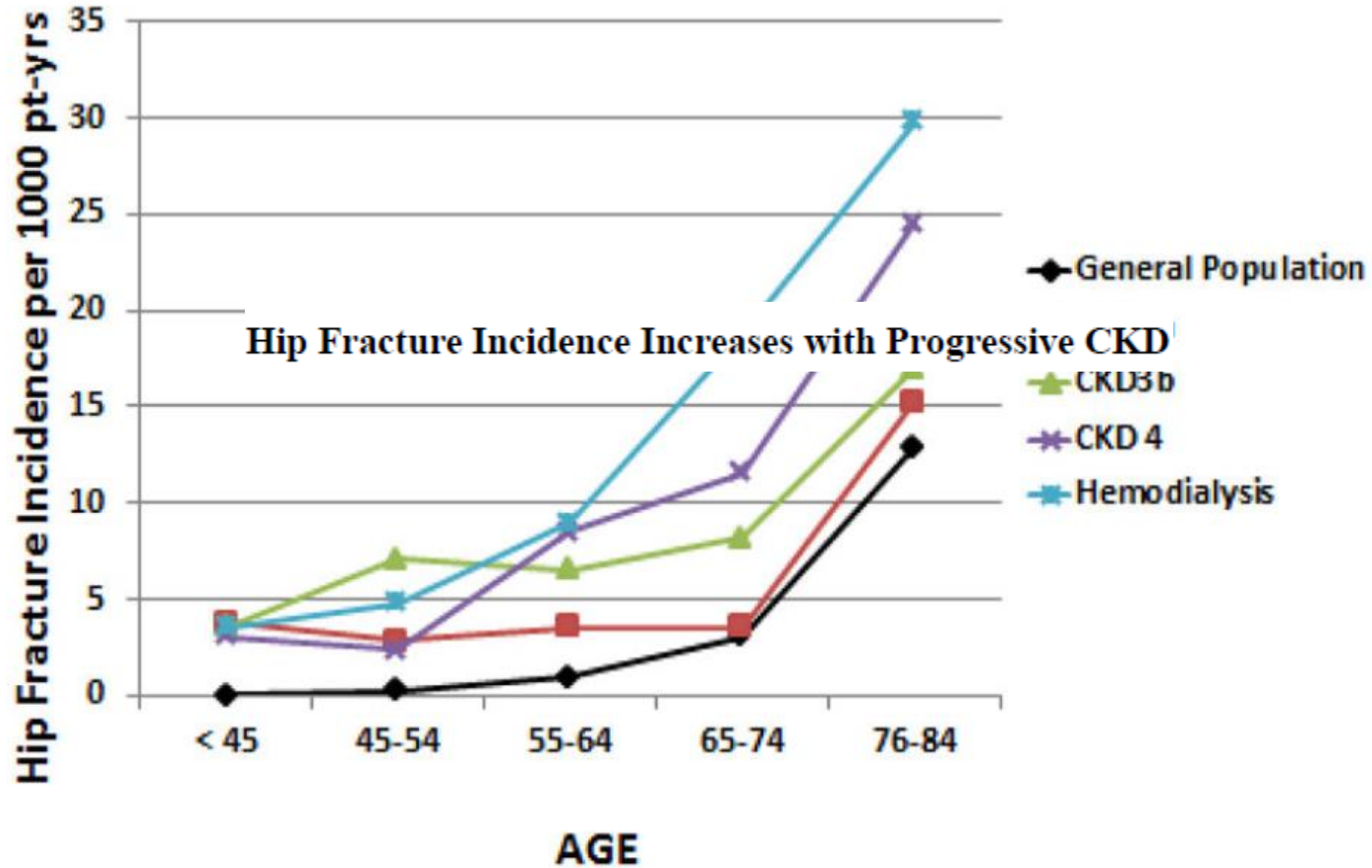
Kidney induced osteoporosis(KIOP)

- ROD and fractures related to kidney disease be considered as a subtype of osteoporosis ,analogous to steroid induced osteoporosis.

Premature aging in CKD

- Assessments of bone health in the general population with tools such as BMD and FRAX risk assessment appear to be relevant in patients with CKD.
- The presence of CKD likely increases the fracture risk above that assessed by these tools and should be regarded as an independent risk factor for fracture, similar to how CKD is now considered an independent risk factor for cardiovascular disease.
- Fractures are one of many 'premature aging' consequences observed in patients with CKD.

Hip Fracture Incidence Increases with Progressive CKD



Assessment of Bone Quality and Fracture Risk in CKD

- Bone biopsy is the gold standard for assessing bone quality in kidney disease and informs treatment options .
- However, its utility as an everyday clinical tool is limited by lack of availability and long duration of time required to process and analyze bone tissue.

Noninvasive Assessment of Bone Quality and Fracture Risk in CKD

Imaging modalities such as

- DXA
- Trabecular bone score (TBS)
- Conventional Quantitative computed tomography (QCT)
- High-resolution peripheral QCT (HRpQCT)
- Micro magnetic resonance imaging (MRI)

Assess bone density and/or structural aspects of bone quality

Assessment of Bone Quality and Fracture Risk in CKD

- Historically the role of DXA to assess bone health and fracture risk in CKD3-5D was controversial.
- Several recent longitudinal studies in patients across the spectrum of CKD and ESKD have demonstrated that low **BMD at the hip and forearm do predict incident fractures.**
- These studies reported that the WHO T-scores perform similarly in patients with and without CKD, with regard to fracture prediction, and resulted in the revised KDIGO recommendation to include BMD measurement in patients with CKD 3-5D to assess fracture risk.

Limitations of DXA

- An important limitation of DXA is that it does not assess the 3-dimensional structure of bone.
- The interpretation of DXA may be confounded by the presence of extraosseous calcification and focal areas of osteosclerosis, which may lead to artifactual increase in BMD

Sever osteoarthritis results to false elevated BMD of spine

Vala Bone Densitometry Center
Unit 10, No. 85, 3rd Floor, 2nd Golestan st., Pasdaran Ave.
Tehran, Iran

Telephone: +98-21-26653587

E-Mail: valabmd@gmail.com

Fax: +98-21-26653584

Name: Khatzian, Gholia 13/1/1998
Patient ID: 40202200J
DOB: 26 May 1990

Sex: Female
Ethnicity: Caucasian
Menopause: Age: 59

Height: 165.0 cm
Weight: 68.0 kg
Age: 79

Referring Physician: Dr.Zabihi Yeganeh

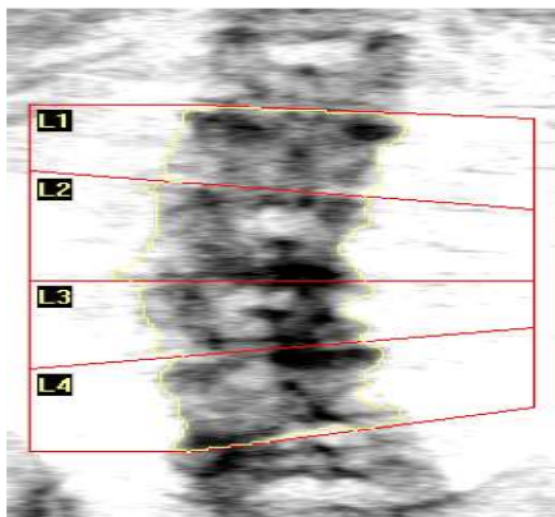


Image not for diagnostic use
116 x 127

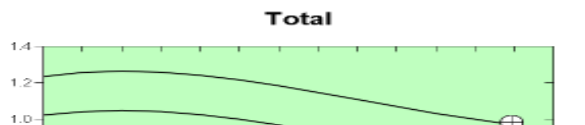
Scan Information:

Scan Date: 02 February 2020 ID: A0202200J
Scan Type: f Lumbar Spine
Analysis: 02 February 2020 16:37 Version 13.6.0.5
Spine
Operator: A.A
Model: Horizon Wi (S/N 301656M)
Comment:

DXA Results Summary:

Region	Area (cm ²)	BMC (g)	BMD (g/cm ³)	T - score	PR (%)	Z - score	AM (%)
L1	14.42	13.57	0.941	-0.4	95	1.9	129
L2	16.24	15.51	0.955	-0.7	93	2.0	129
L3	12.70	12.90	1.016	-0.6	94	2.1	130
L4	15.30	15.77	1.031	-0.3	97	2.6	138
Total	58.66	57.75	0.985	-0.6	94	2.1	131

Total BMD CV 1.0%
WHO Classification: Normal
Fracture Risk: Not Increased

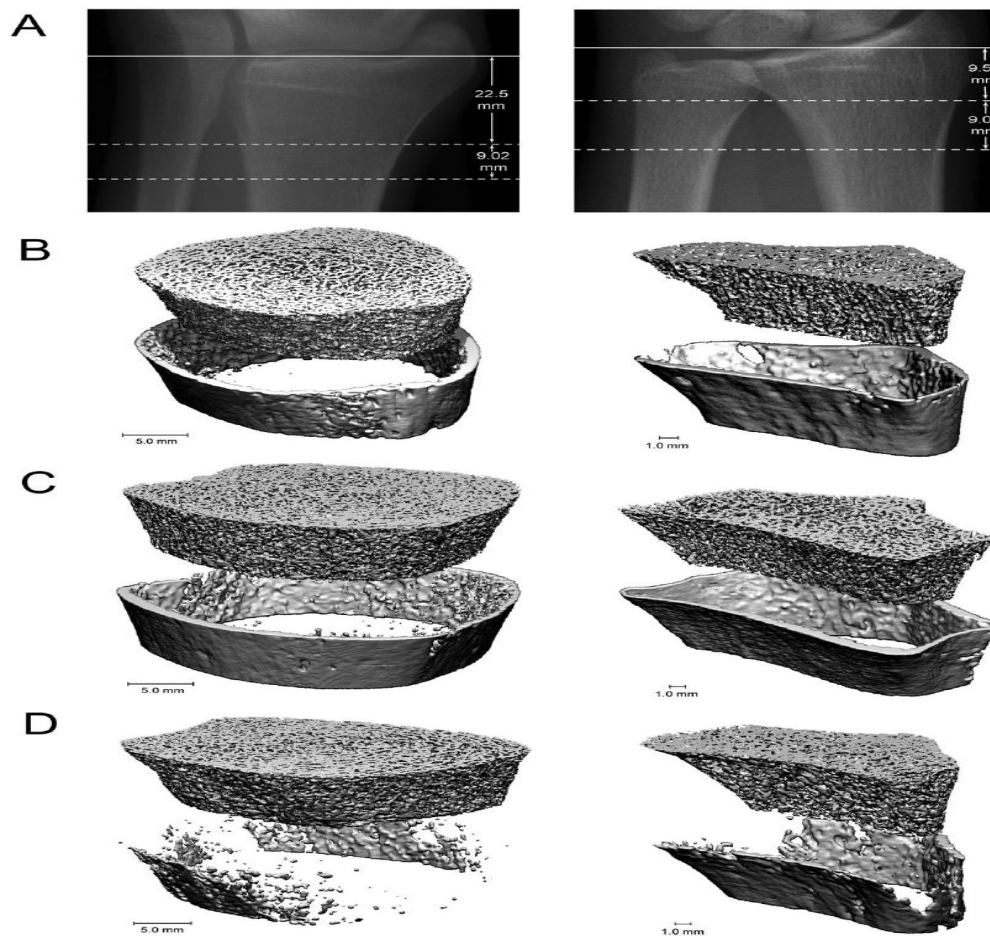


QCT

- High-resolution imaging methods such as QCT, HR-pQCT, and micro-MRI have been developed to provide 3-dimensional imaging of bone density and microarchitectural aspects of bone quality, including cortical and trabecular volumetric BMD, geometry, microarchitecture, and strength.
- In CKD and ESKD, studies utilizing QCT have shown that cortical deficits predominate and these could discriminate and predict future fractures.

- HR-pQCT has a higher nominal resolution, which allows for quantification of trabecular number, thickness, and separation
- Finite element analysis (FEA) has been used in biomechanics to determine the mechanical behavior (and therefore strength) of bone.
- The advent of high-resolution imaging has allowed FEA to be used in the assessment of bone strength, stiffness, and failure load, either in its entirety or in individual (cortical or trabecular) compartments.

HR-pQCT provides detailed images of bone microarchitecture at the radius (left) and tibia (right). Scout view (A) reference line position (solid line) and the measurement site (dotted line). Images from healthy, postmenopausal white female (B). Images from female with CKD, no fractures (C). Images from female with CKD and prevalent fractures (D).



The use of HR-pQCT in the clinic is not currently practical because of cost and limited availability.

Criteria of osteoporosis

- WHO BMD criteria for osteoporosis can be used in patients with stages 1–3 CKD, the disorders of bone turnover become so aberrant by stages 4 and 5 CKD that the WHO criteria can not be used for the diagnosis of osteoporosis.
- NOF criteria (National osteoporosis foundation)
 - Include vertebral image and FRAX plus T score

TABLE III Patients Meeting WHO or NOF Criteria

	Female (N = 102)	Male (N = 20)	Total (N = 122)
WHO criteria			
Normal (≥ -1.0 point)	3%	10%	4%
Osteopenia (-2.4 to -1.1 points)	52%	70%	55%
Osteoporosis (≤ -2.5 points)	45%	20%	41%
NOF criteria			
T-score of ≤ -2.5 at the hip, spine, or wrist	45%	20%	41%
T-score of -2.4 to -1.1 points at hip or spine and high FRAX risk	45%	60%	48%
History of hip or spine fracture (n = 70)	24%	30%	43%
Meeting at least 1 criterion	92%	85%	91%

COPYRIGHT © 2020 BY THE JOURNAL OF BONE AND JOINT SURGERY, INCORPORATED

Bone Health Optimization in Orthopaedic Surgery

Aamir Kadri, MS, Neil Binkley, MD, Kristyn J. Hare, MMS, PA-C, and Paul A. Anderson, MD

Investigation performed at the University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin

DXA of the hip. Sixty-seven-year-old woman with previous fracture of the distal radius. Femoral neck T-score is -2.3, which is in the osteopenic range. This is an ideal patient for FRAX®. Because the 10-year-risk of hip fracture exceeds 3 %, this patient meets the National Osteoporosis Foundation guidelines for pharmacologic therapy

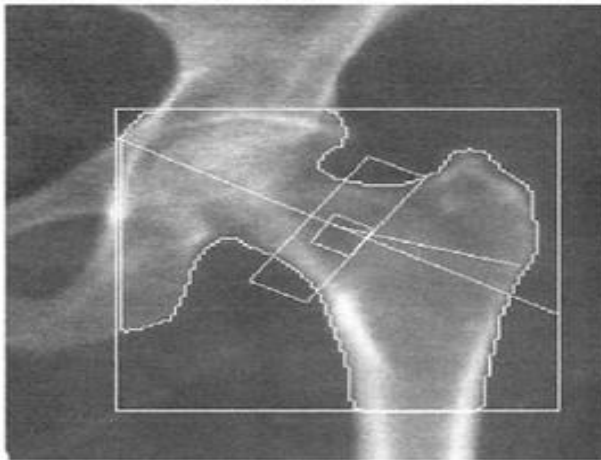


Image not for diagnostic use
k = 1.149, d0 = -46.8
94 x 100
NECK: 49 x 15

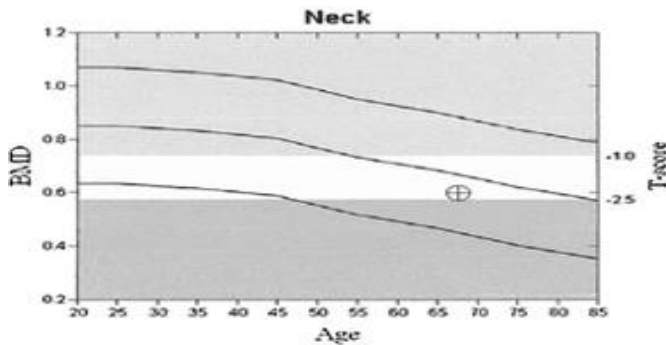
Scan Information:

Scan Date: February 29, 2012
Scan Type: a Left Hip
Analysis: February 29, 2012 14:17 Version 13.3:3
Hip
Operator: SH
Model: Discovery A (S/N 70314)
Comment: FV3-

DXA Results Summary:

Region	Area (cm ²)	BMC (g)	BMD (g/cm ³)	T - score	PR (%)	Z - score	AM (%)
Neck	5.02	3.00	0.596	-2.3	70	-0.6	90
Troch	9.72	6.03	0.621	-0.8	88	0.4	107
Inter	17.14	18.18	1.061	-0.3	96	0.9	114
Total	31.88	27.21	0.854	-0.7	91	0.6	110

Total BMD CV 1.0%, ACF = 1.025, BCF = 1.008, TH = 6.208
WHO Classification: Osteopenia



FRAX® WHO Fracture Risk Assessment Tool

10-year Fracture Risk ¹	
Major Osteoporotic Fracture	19%
Hip Fracture	3.6%
Reported Risk Factors: US (Caucasian), T-score(WHO)=-2.2, BMI=31.9, previous fracture	

¹ FRAX® Version 3.01. Fracture probability calculated for an untreated patient. Fracture probability may be lower if the patient has received treatment.

Comment:

All treatment decisions require clinical judgment and consideration of individual patient factors, including patient preferences, comorbidities, previous drug use and risk factors not captured in the FRAX model (e.g. frailty, falls, vitamin D deficiency, increased bone turnover, interval significant decline in BMD).

Indications for BMD Testing

Adults with a condition (e.g., rheumatoid arthritis) or taking a medication (e.g., glucocorticoids in a daily dose ≥ 5 mg prednisone or equivalent for \geq three months)

Women age 65 and older and men age 70 and older, regardless of clinical risk factors

Younger postmenopausal women, women in the menopausal transition and men age 50 to 69 with clinical risk factors for fracture

Adults who have a fracture after age 50













Vertebral imaging

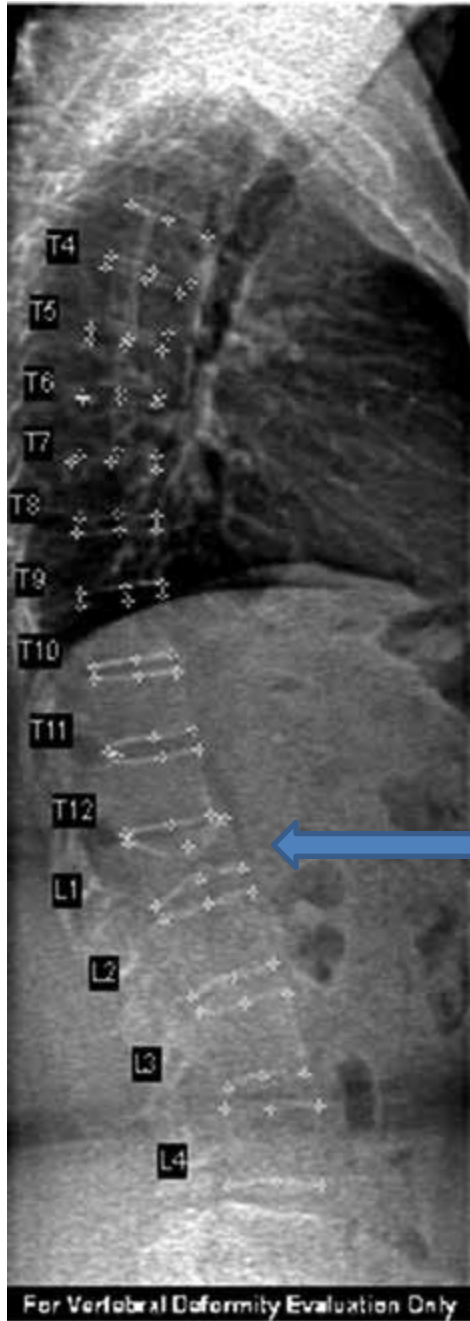
- A vertebral fracture (VF) is consistent with a diagnosis of osteoporosis, even in the absence of a bone density diagnosis.
- (VF) is an indication for pharmacologic treatment with osteoporosis medication to reduce subsequent fracture risk.

Consider vertebral imaging tests

- All women age 70 and older and all men age 80 and older if BMD T-score at the spine, total hip or femoral neck is < -1.0 .
- Women age 65 to 69 and men age 70 to 79 if BMD T-score at the spine, total hip or femoral neck is < -1.5 .
- Postmenopausal women and men age 50 and older with specific risk factors:
 - Low trauma fracture during adulthood (age 50)
 - Historical height loss of 1.5 inches or more (4 cm)
 - Prospective height loss of 0.8 inches or more (2 cm)
 - Recent or ongoing long term glucocorticoid treatment

Semiquantitative (SQ) Grading for Vertebral Fractures

0	Normal			
0,5	<i>Uncertain or questionable vertebrae</i>			
1	Mild Fracture 20-25 %	 anterior	 middle	 posterior
2	Moderate Fracture 25-40%	 anterior	 middle	 posterior
3	Severe Fracture > 40%	 anterior	 middle	 posterior



**IVA/VFA report:
L1 severe biconcave fx**

Examples of VFA Images with Inadequate Space (Left Panel) and Adequate Space (Right Panel) Anterior to the Aorta for AAC Assessment.



Schousboe JT, Wilson KE, Hangartner TN (2007) Detection of Aortic Calcification during Vertebral Fracture Assessment (VFA) Compared to Digital Radiography. PLOS ONE 2(8): e715. <https://doi.org/10.1371/journal.pone.0000715>
<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0000715>

Micro architecture survey

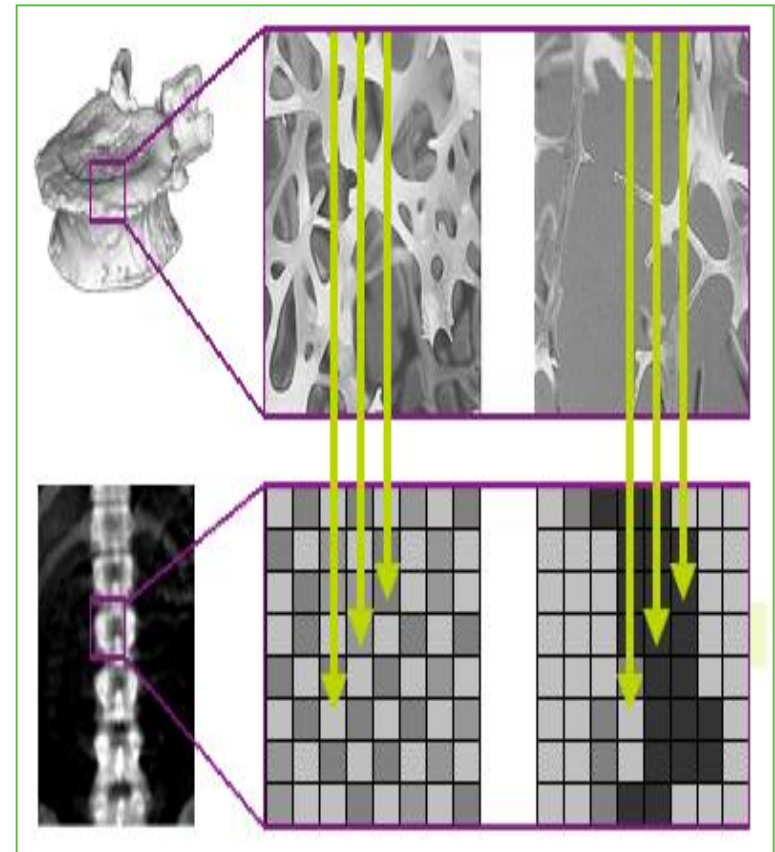
- Osteoporosis is a skeletal disorder characterized by *both low bone density & micro architectural deterioration.*
- Prevention of osteoporotic fracture, needs paying attention to the both surrogates of bone strength.

Introduction

- Until recently, aBMD was the only method used in assessment of osteoporosis and fracture risk.
 - more than half of the fragility fractures occurred in people with aBMD above the diagnostic threshold of osteoporosis.
- TBS has recently been shown to independently predict fracture risk, to complement standard aBMD imaging.

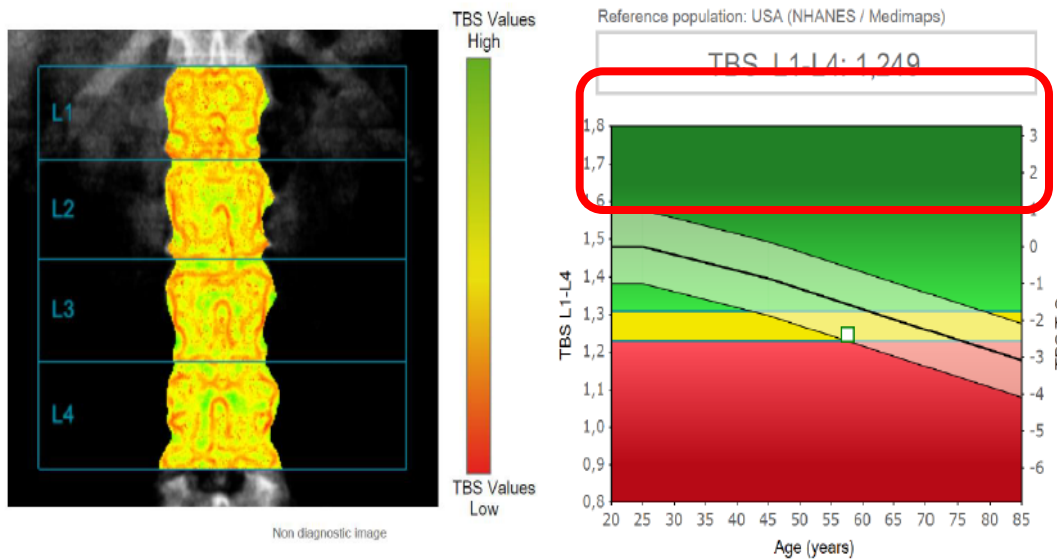
Introduction

- TBS uses standard DXA spine images to measure texture in-homogeneity that is, how well-structured or poorly structured the trabecular bone appears when assessed as individual voxels and local variations in gray level distribution.



What is TBS?

- TBS is an advanced imaging **software** provided for use as a complement to DXA.
- TBS score is related to the **bone microarchitecture** and the **fracture risk**.



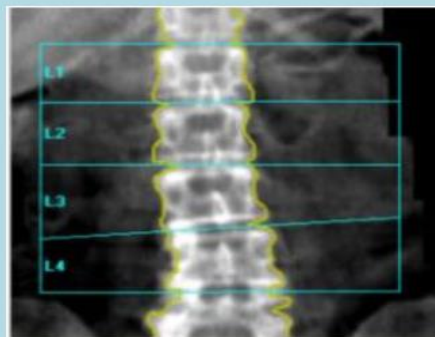
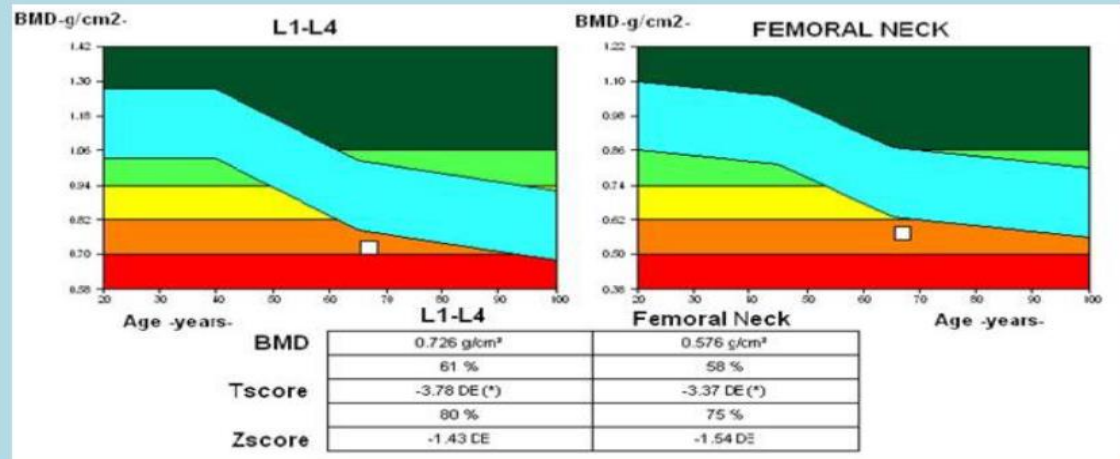
Fracture risk level based on TBS of the spine		
	Intermediate (partially degraded)	Low (degraded)
High (normal)	≤ 1.310 and > 1.230	≤ 1.230
> 1.310		

70 years old patient with low BMD and low TBS recommend an antiresorptive treatment with alendronate

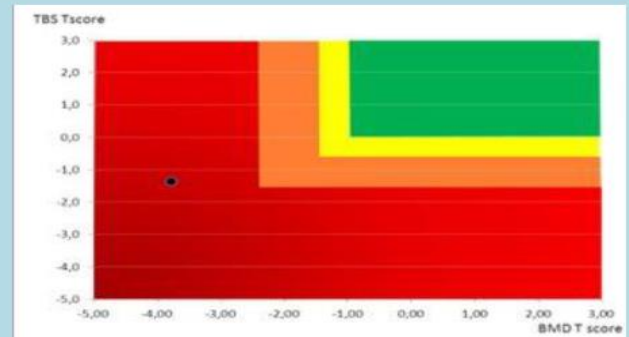
Bone Assessment & Analysis Images



LVA:
No observed height loss in vertebral bodies at T4-L4 region suggesting deformities or fractures.



BMD:
Lumbar Spine showed light degenerative changes.

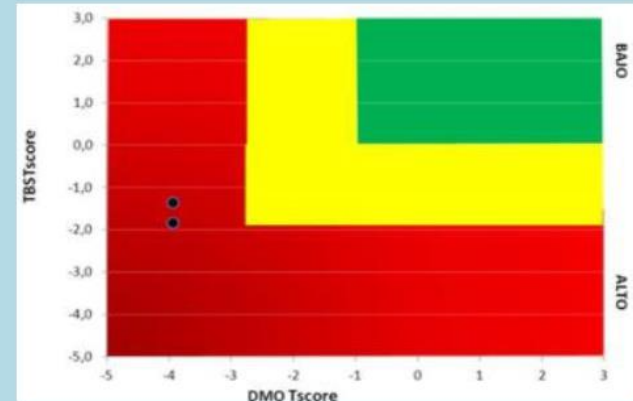
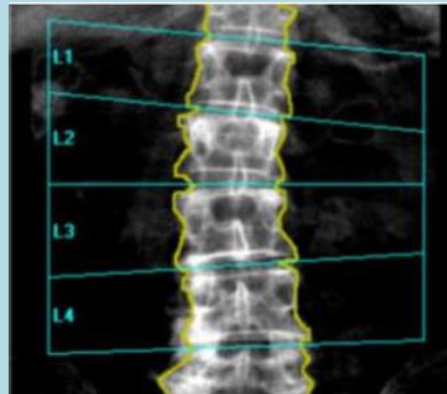
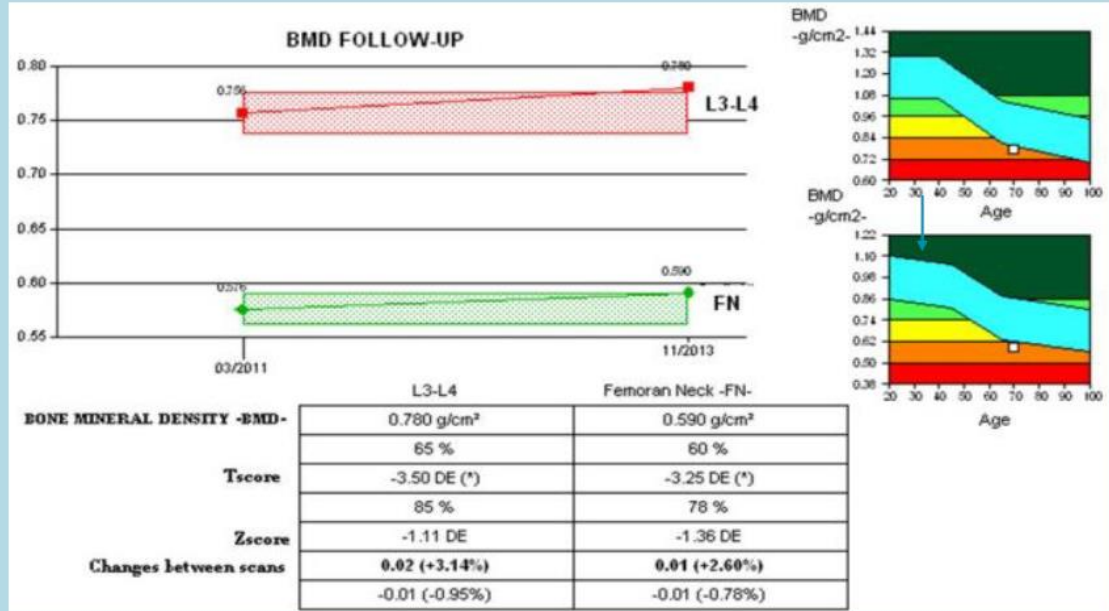
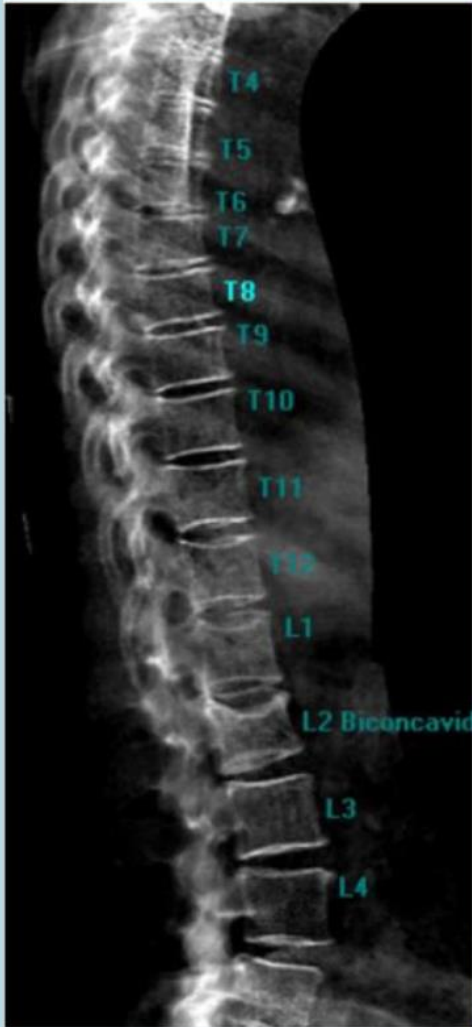


TBS / BMD:
Combined TBS and BMD results are in the zone of high compromise in bone structure and density.

Follow up

- She came back for control after 2 years. Weight and height were similar (Weight: 55kg; Height: 158cm), she did not suffer any fall in the meantime.
- A DXA scan was performed and changes in the image of L2 at lumbar spine were noted.
- A new LVA was also acquired.
- The lumbar spine BMD showed an increase (+3.14%), as well as in the femoral neck (+2.60%) with respect to initial scans.

Very high risk for fracture despite increased BMD notice deterioration of TBS



FRAX

Clinical risk factors for fracture

Advancing age
Previous fracture
Glucocorticoid therapy
Parental history of hip fracture
Low body weight
Current cigarette smoking
Excessive alcohol consumption
Rheumatoid arthritis
Secondary osteoporosis (eg, hypogonadism or premature menopause, malabsorption, chronic liver disease, inflammatory bowel disease)

Data from: Kanis JA, Borgstrom F, De Laet C, et al. Assessment of fracture risk. *Osteoporos Int* 2005; 16:581.

Assessment of fracture risk

- In clinical practice, FRAX may be applied to patients with CKD.
- FRAX does not include any adjustment of risk according to GFR.
- Clinician should also consider adjusting the absolute fracture risk to a higher level (approximately double) in patients with eGFR stages G3b to G5.

FRAX

- In US, the gateway to treatment includes either a prior fracture (hip or spine fracture) or a BMD *T score of ≤ -2.5 SD* irrespective of FRAX.
- FRAX is reserved for individuals in whom the *T score is in the osteopenic range and* treatment recommended if the probability of a major fracture or hip fracture lies at 20% or more or 3% or more, respectively.

CaucasiaCaucasian woman, 58 years, smoker

Calculation Tool

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

Country: **UK** Name/ID: [About the risk factors](#)

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth
Age: Date of Birth: Y: M: D:

2. Sex Male Female

3. Weight (kg)

4. Height (cm)

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/cm²)
T-Score

BMI: 25.4
The ten year probability of fracture (%)
with BMD

Major osteoporotic	9.1
Hip Fracture	3.1
View NOGG Guidance	

If you have a TBS value, click here:



Weight Conversion

Pounds kg

Height Conversion

Inches cm

02765050

Individuals with fracture risk assessed since 1st June 2011

www.nos.org.uk



[Print tool and information](#)

Caucasian woman, 58 years, smoker

Calculation Tool

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

Country: **UK** Name/ID: [About the risk factors](#)

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth
Age: Date of Birth: Y: M: D:

2. Sex Male Female

3. Weight (kg)

4. Height (cm)

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/cm²)
T-Score

BMI: 25.4
The ten year probability of fracture (%)

with BMD

Major osteoporotic	9.1
Hip Fracture	3.1

[View NOGG Guidance](#)

here:

TBS Adjustment



Weight Conversion

Pounds kg

Height Conversion

Inches cm

02765050

Individuals with fracture risk assessed since 1st June 2011


www.nos.org.uk



[Print tool and information](#)

CaucasianCaucasian woman, 58 years

FRAX adjusted for TBS



WHO FRAX web site
What is TBS?
Calculation Tool
References
TBS web site

Calculation tool

Low TBS = 1.16

Country: UK

Name/ID: N/A

Age: 58

Sex: Female

BMI (kg/m²): 25.4

Please enter the Trabecular Bone Score to compute the ten year probability of fracture adjusted for TBS

Lumbar Spine TBS:

Attention: TBS values are accurate only for patients (women and men) with a BMI in the range [15 – 37 kg/m²]

**Before
TBS Adjustment**

BMI: 25.4

The ten year probability of fracture (%)

with BMD

Major osteoporotic	9.1
Hip Fracture	3.1

[View NOGG Guidance](#)

The 10 year probability of fracture (%)
Adjusted for TBS

Major Osteoporotic Fracture: 12

Hip Fracture: %

4 %

**After
TBS Adjustment**

00000026

Individuals with fracture risk assessed since 1st March 2015

TBS

- Data support the use of the TBS adjustment of AFR through the FRAX[®] algorithm in subjects with CKD.
- There is limited data on TBS in CKD.
- TBS was associated with fractures independent of the FRAX[®] score including BMD.

FRAX limitations

- High, moderate, and low exposure to glucocorticoids
- Concurrent data on lumbar spine BMD
- Information on trabecular bone score (TBS)
- Hip axis length
- Falls history
- Immigration status
- Type 2 diabetes
- **Chronic kidney disease**
- Recency of vertebral fracture
- Socioeconomic status
- Variation in body composition

Recency of vertebral fracture

- The most recent FRAX adjustment was related to the recency of vertebral fracture.
- Risk of a subsequent osteoporotic fracture is particularly acute immediately after the index fracture (first 2 years)and wanes progressively with time.

Take home message

- KIO, is associated with an increased risk of fragility fractures.
- Assessment of Bone Quality and Fracture Risk in CKD besides DXA with a practical tool.
 - low BMD at the hip and forearm do predict incident fractures.
 - DXA pitfalls (aortic calcification and severe osteoarthritis).
 - TBS can predict fracture independent of BMD.
 - Vertebral Fracture assessment by xray or VFA-DXA is important for decision making in particular situation and detection of asymptomatic vertebral FX.
 - Frax should be adjusted in ckd patients.