Diabetes & Bone Health: A Forgotten Complication

Julie Gilmour, MBChB, FRCPC, MSc(HQ)
February 6th, 2018
Beyond The Break
Disclosures

Relevant relationships with commercial entities
  • None

Potential for conflicts of interest within this presentation
  • None
Outline

1. What is the risk of fracture in individuals with Diabetes Mellitus (DM)?
2. What are the mechanisms for bone fragility in DM?
3. How do we assess the risk of fracture in individuals with DM?
4. Does glycemic control have an impact on bone health and fracture risk?
5. How do DM medications impact bone health?
6. What strategies exist for preventing and treating osteoporosis in individuals with DM?
CASE 1

- 52 year old male with T1 DM, A1C 7.2%, BMI 20
- Diagnosed with T1 DM at age 5
- History of wrist fracture at age 30 playing hockey
- Complications:
  - Peripheral neuropathy
  - Background retinopathy
- Treatment:
  - MDI insulin (Glargine and Humalog)

Questions to consider:
- Should this patient be screened for OP with a BMD?
- Do any elements of this patients history put him at increased risk of fracture?
CASE 2

- 64 year old female with T2 DM x 5 years
- A1C 9%, BMI 30, no previous fracture
- Complications
  - History of nephropathy - ACR 10, eGFR > 60
- Medications:
  - Metformin 1g bid
  - Sitagliptin 100mg daily
  - Canagliflozin 300mg po daily
  - Patient has refused insulin

Questions to consider:
- Would you expect her BMD to be low, normal, or high?
- Do any elements of this patients history put her at increased risk of fracture?
Outline

1. What is the risk of fracture in individuals with Diabetes Mellitus (DM)?

2. What are the mechanisms for bone fragility in DM?

3. How do we assess the risk of fracture in individuals with DM?

4. Does glycemic control have an impact on bone health and fracture risk?

5. How do DM medications impact bone health?

6. What strategies exist for preventing and treating osteoporosis in individuals with DM?
Osteoporosis: Definition

• A systemic skeletal disorder characterized by decreased bone strength
• Resulting in an increase risk of fragility fracture
• WHO definition:
  • Osteoporosis: DXA T-score <= -2.5

Solomon, NEJM, Jan 2016
Osteoporosis Canada website
What contributes to bone strength?

1. Architecture
   • Geometry (Size/Shape)
   • Microarchitecture
2. Turnover/Remodeling
3. Damage Accumulation
   • Microfracture
4. Mineralization
5. Bone Matrix
   • Collagen (type/crosslinks)

NIH Consensus Development Panel on OP. JAMA 2001
How common is an Osteoporotic Fracture in the General Population?

- 1 in 3 women and 1 in 5 men will suffer an osteoporotic fracture in their lifetime

- Over 80% of all fractures in people over 50 years are due to osteoporosis
Increased Risk of Hip Fracture in Individuals with DM

Increased Peripheral Fractures in DM

93,676 women followed prospectively for 7 years
• Women’s Health Initiative Observational Cohort

<table>
<thead>
<tr>
<th>Fractures per 1,000 person-yr (n)</th>
<th>T2 DM</th>
<th>No DM</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any fracture</td>
<td>28.6 (899)</td>
<td>22.0 (12,575)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hip/pelvis/upper leg</td>
<td>3.8 (128)</td>
<td>2.5 (1,531)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Lower leg/ankle/knee</strong></td>
<td><strong>6.2 (207)</strong></td>
<td><strong>4.7 (2,828)</strong></td>
<td><strong>0.0001</strong></td>
</tr>
<tr>
<td>Foot</td>
<td>4.6 (153)</td>
<td>3.2 (1,940)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Upper arm/shoulder/elbow</td>
<td>3.8 (129)</td>
<td>2.8 (1,717)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Lower arm/wrist/hand</td>
<td>5.3 (177)</td>
<td>5.2 (3,161)</td>
<td>0.83</td>
</tr>
<tr>
<td>Spine/tailbone</td>
<td>2.9 (99)</td>
<td>2.2 (1,336)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Bonds et al. JCEM 2006; 91:3404–3410
Outline

1. What is the risk of fracture in individuals with Diabetes Mellitus (DM)?

2. What are the mechanisms for bone fragility in DM?

3. How do we assess the risk of fracture in individuals with DM?

4. Does glycemic control have an impact on bone health and fracture risk?

5. How do DM medications impact bone health?

6. What strategies exist for preventing and treating osteoporosis in individuals with DM?
Pathophysiology of Bone Fragility and Fracture in DM

1. Decreased bone formation
2. Increased bone resorption
3. Decreased bone quality
4. Increased propensity to fall
Osteoblast

- Bone forming cell
- Lay down collagen and induce mineralization

Decreased Bone Formation in DM

1. Hyperglycemia leads to the formation of AGE
   = Apoptosis of mesenchymal stem cells
   = Prevent maturation/function of osteoblast

2. Hyperglycemia leads to altered expression of genes needed for osteoblastogenesis
   = Adipogenesis favoured over bone formation

3. Decreased Wnt Signalling
   = Due to increased sclerostin
   = Reduction in osteoblastic synthesis
Mesenchymal Stem Cell differentiation

WNT Signaling

Sclerostin increased from osteocyte in DM

Sclerostin Inhibits WNT signaling

Increased sclerostin levels have been associated with vertebral fractures in T2 DM


Yamamoto et al. JCEM 2013; 98(10):4030–4037
Pathophysiology of Bone Fragility and Fracture in DM

1. Decreased bone formation
2. Increased bone resorption
3. Decreased bone quality
4. Increased propensity to fall
Osteoclast

- Responsible for bone resorption
- Does this following stimulation RANKL
- Secretes acid onto bone surface – dissolves bone mineral
- Secretes enzymes - that breaks down collagen

Increased Bone Resorption in DM

1. Increased osteoclast number and function
   - Altered signaling from osteoblast = decreased osteoprotegerin (OPG)
   - Inflammation = Increased TNF-a & IL-6

- Thought to be a less prominent effect/conflicting results (may occur later in the pathophysiology of the disease)
Osteoclastic Bone Resorption

Inflammatory Cytokines

Osteoclastogenic cytokines:
IL-1, IL-6, TNF, IL-8, IL-11, IL-15, IL-17, IL-32

Anti-osteoclastogenic cytokines:
IFN-γ, IFN-β, IFN-α, IL-4, IL-10, IL-13, IL-18, IL-33

Activation of osteoclasts:
cathepsin K, TRAP, calcitonin receptor, OSCAR, β3 integrin

Bone

RANK/RANKL/OPG

Nature Medicine 2007
Biochimia Medica 2013
Pathophysiology of Bone Fragility and Fracture in DM

1. Decreased bone formation
2. Increased bone resorption
3. Decreased bone quality
4. Increased propensity to fall
Pathway of non-enzymatic cross-link formation in bone collagen

Normal enzymatic cross-linking in collagen gives bone its toughness and scaffolding properties.

AGE cross-links lead to biomechanically that is less able to deform before fracturing.

Nuti et al. Nutrition, Metabolism & Cardiovascular Diseases (2010) 20, 683-690
Yamamoto et al. JCEM 2013; 98(10):4030–4037
Pathophysiology of Bone Fragility and Fracture in DM

1. Decreased bone formation
2. Increased bone resorption
3. Decreased bone quality
4. Increased propensity to fall
Increased Risk of Falls in Diabetes

- Increased risk of falls with T2 DM
  - Meta-analysis (8 studies) increased falls risk of 1.19 (1.08-1.31) comparing DM vs. no DM

- Insulin-treated T2 DM
  - Even higher risk – 2-3x increased risk compared to non-DM

- Rotterdam Study – falls not the entire story for increased fracture!
  - Non-vertebral fracture risk for treated T2DM (adjusted for falls): HR = 1.69 (95% CI 1.16–2.46)

Why is there an increased risk of falls?

- Thought to be related to an increased likelihood of
  - Peripheral neuropathy
  - Autonomic neuropathy (postural hypotension)
  - Hypoglycemia
  - Poor vision: retinopathy/cataracts
  - Stroke
Other Mechanisms of Bone Fragility

1. Glycosuria
   • Favours hypercalciuria which leads to a negative calcium balance

2. Lack of insulin has a catabolic effect on bone
   • Lower peak bone mass achieved in T1 DM
     • Especially if develop T1 DM before puberty
   • Hyperinsulinemia in T2 DM promotes bone formation and differentiation of osteoblast

3. Low Vitamin D

4. Decreases in IGF-1

5. Poor vasculature to the cortical bone

Compston et al. JIM. 2018
Outline

1. What is the risk of fracture in individuals with Diabetes Mellitus (DM)?
2. What are the mechanisms for bone fragility in DM?
3. How do we assess the risk of fracture in individuals with DM?
4. Does glycemic control have an impact on bone health and fracture risk?
5. How do DM medications impact bone health?
6. What strategies exist for preventing and treating osteoporosis in individuals with DM?
The same way we assess fracture risk in the non-DM population

CAROC & FRAX

Any differences?
Individuals with T1 DM should be screened for Osteoporosis at age 50

**Indications for BMD Testing**

<table>
<thead>
<tr>
<th>Older Adults (age ≥ 50 years)</th>
<th>Younger Adults (age &lt; 50 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- All women and men age ≥ 65 years</td>
<td>- Fragility fracture</td>
</tr>
<tr>
<td>- Menopausal women, and men aged 50-64 years with clinical risk factors for fracture: Fragility fracture after age 40</td>
<td>- Prolonged use of glucocorticoids*</td>
</tr>
<tr>
<td>- Prolonged glucocorticoid use†</td>
<td>- Use of other high-risk medications†</td>
</tr>
<tr>
<td>- Other high-risk medication use*</td>
<td>- Hypogonadism or premature menopause</td>
</tr>
<tr>
<td>- Parental hip fracture</td>
<td>- Malabsorption syndrome</td>
</tr>
<tr>
<td>- Vertebral fracture or osteopenia identified on X-ray</td>
<td>- Primary hyperparathyroidism</td>
</tr>
<tr>
<td>- Current smoking</td>
<td>- Other disorders strongly associated with rapid bone loss and/or fracture</td>
</tr>
<tr>
<td>- High alcohol intake</td>
<td></td>
</tr>
<tr>
<td>- Low body weight (&lt; 60 kg) or major weight loss (&gt; 10% of weight at age 25 years)</td>
<td></td>
</tr>
<tr>
<td>- Rheumatoid arthritis</td>
<td></td>
</tr>
<tr>
<td>- Type 1 diabetes, osteogenesis imperfecta, uncontrolled hyperthyroidism, hypogonadism or premature menopause (&lt; 45 years), Cushing's disease, chronic malnutrition or malabsorption, chronic liver disease, COPD and chronic inflammatory conditions (e.g., inflammatory bowel disease)</td>
<td></td>
</tr>
</tbody>
</table>

*≥3 months in the prior year at a prednisone equivalent dose ≥ 7.5 mg daily; *e.g., aromatase inhibitors, androgen deprivation therapy.
DM and BMD

- In T1 DM – BMD is low
  - 20% of patients age 20–56 with T1 DM meet BMD criteria for osteoporosis

- In T2 DM – BMD is relatively high or normal
  - Paradoxical increased # risk
    - Increased risk of falls
    - Poor bone quality (microarchitecture)
  - High BMD postulated to be related to:
    - Increased weight and mechanical loading of bone
    - Overestimation due to increased BMI
  - BMD predicts risk of fracture, but underestimates the overall risk

Microarchitecture Includes:

1. Trabecular architecture
2. Cortical thickness and porosity
Two Types of Bone

M = marrow

Methods to Assess Bone Microarchitecture

- Bone biopsy
- CT
- MRI
- Trabecular Bone Score
What is TBS?

Texture Parameter – records pixels by gray-level variations in DXA image

A low TBS value indicates few gray-level variations of large amplitude and is interpreted as low quality of bone texture

Introduced in 2008 by Pothuaud et al. (Bone)
BMD = 0.972

Illustration of Well-structured trabecular bone

TBS = 1.459

BMD = 0.969

Illustration of Altered trabecular bone

Experimental variogram

TBS = 1.243
Risk Classification has been Suggested in Post-Menopausal Female Population

- $> 1.35 = \text{normal}$
- $1.2 - 1.35 = \text{partially degraded microarchitecture}$
- $< 1.2 = \text{degraded microarchitecture}$

TBS Can Now Be Incorporated Into FRAX Assessment
T2 DM & Mechanical Bone Properties

• Cortical bone is compromised in DM (most studies)
  • Some evidence that this may be due to altered blood supply to this layer

• Imaging techniques:
  • BMD high or normal
  • HRpQCT – increased porosity of cortical bone, decreased cortical area, no change in trabecular microarchitecture
  • Reduced trabecular bone score (TBS)

T2 DM has an Impairment in Cortical Bone

Control

T2 DM

T2 DM with fracture

Andrew J. Burghardt; Ahi S. Issever; Ann V. Schwartz; Kevin A. Davis; Umesh Masharani; Sharmila Majumdar; Thomas M. Link; *The Journal of Clinical Endocrinology & Metabolism* **2010**, *95*, 5045-5055.
TBS in T2 DM

- Dhaliwal et al – 57 women with T2 DM compared to 43 healthy controls
  - TBS was lower and BMD was higher in DM ($p = 0.001$ and 0.01)
  - A1C $< 7.5\%$ vs $> 7.5\%$
    - BMD unchanged
    - TBS was lower with poorer control

- Leslie et al – 2356 women over 50 years with DM compared to those without DM (retrospective cohort)
  - Women with DM more likely to be in the lowest 1/3 of TBS values
  - TBS and BMD were predictive of fracture (independently)

T1 DM & Mechanical Properties of Bone

• Little research

• Imaging techniques:
  • MRI – reduced trabecular number
  • TBS unchanged in those with and without T1 DM

TBS in T1 DM

- 119 T1 DM vs 68 controls, cross-sectional
- T1 patients vs controls – no stat. significant difference in TBS
- T1 fracture vs T1 no fracture – TBS 1.3 vs 1.37
  - 25 had prevalent fractures
- TBS cut-off of 1.42 discriminated presence of fracture with a sensitivity of 91.7% and specificity of 43.2%

Neumann et al. Ost Int. 2015
Outline

1. What is the risk of fracture in individuals with Diabetes Mellitus (DM)?

2. What are the mechanisms for bone fragility in DM?

3. How do we assess the risk of fracture in individuals with DM?

4. Does glycemic control have an impact on bone health and fracture risk?

5. How do DM medications impact bone health?

6. What strategies exist for preventing and treating osteoporosis in individuals with DM?
Does Glycemic Control Influence Fracture Risk?

• Debated

• Some observational studies demonstrating an increased fracture risk with frequent hypoglycemic episodes

• Poor glycemic control may be linked to increased fracture risk
  • But intensive lowering of A1C does not reduce fracture risk

Intensive Glycemic Control did Not Increase or Decrease Fracture/Fall Risk in ACCORD

<table>
<thead>
<tr>
<th>Fracture site</th>
<th>Intensive (N = 3,655)</th>
<th>Standard (N = 3,632)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N*</td>
<td>Rate (per 1,000 person-years)‡</td>
</tr>
<tr>
<td>Nonspine</td>
<td>198</td>
<td>13.9</td>
</tr>
<tr>
<td>Hip</td>
<td>11</td>
<td>0.8</td>
</tr>
<tr>
<td>Ankle</td>
<td>44</td>
<td>3.1</td>
</tr>
<tr>
<td>Foot</td>
<td>19</td>
<td>1.3</td>
</tr>
<tr>
<td>Proximal humerus</td>
<td>23</td>
<td>1.6</td>
</tr>
<tr>
<td>Distal forearm</td>
<td>21</td>
<td>1.5</td>
</tr>
</tbody>
</table>

*Number of participants with at least one fracture that occurred after randomization and before the close of the intensive glycemia intervention in February 2008. ‡Rate of first fracture at specific site. †Adjusted for assignment to blood pressure or lipid trial, randomization to blood pressure or lipid intervention, and baseline history of CVD.

Despite increased risk of hypoglycemia in the intensive treatment group (16.2 vs. 5.1%), there was no increased risk of falls.
No difference in BMD between standard and intensive glycemic control groups

<table>
<thead>
<tr>
<th>BMD site</th>
<th>Intensive ((N = 47))</th>
<th>Standard ((N = 58))</th>
<th>Intensive-standard</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total hip</td>
<td>-1.74</td>
<td>-1.12</td>
<td>-0.62 (-3.49 to 2.25)</td>
<td>0.66</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>-3.21</td>
<td>-0.55</td>
<td>-2.66 (-5.93 to 0.62)</td>
<td>0.11</td>
</tr>
<tr>
<td>Lumbar spine</td>
<td>0.55</td>
<td>-0.62</td>
<td>1.17 (-2.35 to 4.69)</td>
<td>0.50</td>
</tr>
<tr>
<td>Whole body</td>
<td>0.12</td>
<td>-0.12</td>
<td>0.24 (-1.41 to 1.89)</td>
<td>0.77</td>
</tr>
</tbody>
</table>
How about POOR Glycemic Control?

A1C 9–10% (HR = 1.24; 1.02–1.49)
A1C 10% + (HR = 1.32; 1.09–1.58)
(compared with A1C 6-7%)

No stat sig difference in <6% vs. 6-7% vs. 7-8%
Does Glycemic Control Influence Fracture Risk?

- Still debated

- Goal:
  - Aim for A1C < 8%, while avoiding hypoglycemia
  - No existing society guidelines on this topic
Outline

1. What is the risk of fracture in individuals with Diabetes Mellitus (DM)?
2. What are the mechanisms for bone fragility in DM?
3. How do we assess the risk of fracture in individuals with DM?
4. Does glycemic control have an impact on bone health and fracture risk?
5. How do DM medications impact bone health?
6. What strategies exist for preventing and treating osteoporosis in individuals with DM?
Classes of Oral Medications Used to Treat DM

- **Negative Impact**
  - TZD
  - Canagliflozin/Dapagliflozin (SGLT-2 inhibitor)

- **Neutral**
  - Metformin
  - Sulphonylurea
  - DPP4-inhibitor
  - GLP-1 inhibitor
  - Empagliflozin (SGLT-2 inhibitor)
TZD

- Activate nuclear hormone PPAR-gamma
- Improve insulin sensitivity in fat tissue
- Examples: Pioglitazone, Rosiglitazone

- What do they do in bone?
  - Shift MSC from osteoblast lineage to adipose cell
  - Increase in osteoblast and osteocyte apoptosis
  - Increase in bone resorption and decrease formation

Gilbert. Endo Reviews. 2015
Figure 2.

TZDs

TZDs → pPAR-γ

Mesenchymal stem cell → Adipocyte

RunX2

Metformin

Osteoblast → Osteoclast

Pramlintide

DPP-4 inhibitors

GIP

GLP-2

Hematopoietic stem cell → Mononucleated Pre-osteoclast → Activated osteoclast

Gilbert. Endo Reviews. 2015
Increased Risk of Fracture in Women on Rosi: ADOPT study

Kahn et al. 2006. ADOPT
TZD Clinical Studies

- Meta-analysis by Loke et al.
  - 10 RCT, 12 months duration
  - 13,000 patients
  - 45% increased risk of fracture
  - Low risk women – 1 fracture per 55 women
  - High risk women – 1 fracture per 21 women

Loke et al. CMAJ. 2009
SGLT-2 Inhibitors

What do we know about SGLT-2 Inhibitors and Fracture?

Canagliflozin

- CANVAS trial
  - 23% increased risk of low trauma fracture (11.6 vs. 9.2 per 1000 patient years, \(p = 0.003\))

Empagliflozin

- EMPA-REG
  - No increased risk of fracture (3.8 vs. 3.9%)
  - Fractures not systemically captured

Compston et al. JIM. 2018
Gilbert. Endocrine Reviews. 2015
What do we know about SGLT-2 Inhibitors and Fracture?

Dapagliflozin

• Pooled analysis of dapagliflozin (Ptaszynska et al, 2014) = No increase in fracture

• Kohan et al, 2014 – investigated dapagliflozin in mild renal impairment (104 weeks)
  • 7.7% fracture in tx group vs none in the placebo group

Compston et al. JIM. 2018
Gilbert. Endocrine Reviews. 2015
Postulated Mechanism of Increased Fracture Risk with SGLT-2 Inhibitors

• Not understood

• Suggested theories:
  1. High serum phosphate $\rightarrow$ secondary hyperparathyroidism
  2. Postural hypotension $\rightarrow$ increased falls
  3. Loss of fat $\rightarrow$ less aromatization $\rightarrow$ less estrogen

Compston et al. JIM. 2018
Outline

1. What is the risk of fracture in individuals with Diabetes Mellitus (DM)?
2. What are the mechanisms for bone fragility in DM?
3. How do we assess the risk of fracture in individuals with DM?
4. Does glycemic control have an impact on bone health and fracture risk?
5. How do DM medications impact bone health?
6. What strategies exist for preventing and treating osteoporosis in individuals with DM?
Non-Pharmalogic Treatment

• **Exercise:**
  • Aerobic – 150min/week
  • Resistance and weight-bearing exercise (2x/week)
  • Balance
    • e.g. yoga and tai chi
    • Daily exercises for ~ 15 min

• Fall prevention strategies – hearing, vision, avoid development of neuropathy

• Assess home for hazards

• Counsel re. smoking cessation, alcohol

Osteoporosis Canada, 2010
Non-Pharmacologic Treatment

• 1200mg/day Calcium
  • Preferred to get in diet – Calcium Calculator
  • Milk, cheese, yogurt, salmon, tofu, sardines

• Under 50 years = 400-1000 IU/day, 50+ years = 800-1000 IU/day of Vitamin D
  • Target blood level >= 75n/mol/L
  • If insufficient/deficient – may need to use higher doses to start
Pharmacologic Therapy Options

• Antiresorptives – prevent bone breakdown
  • Bisphosphonate
  • Rank-ligand inhibitor
  • Estrogen (hormone therapy)
  • Selective estrogen receptor modulator (SERM)

• Anabolic – increases bone formation
  • Teriparatide

• Avoid DM meds that have a negative effect on bone
Bisphosphonates and DM

• There are no RCT’s specifically looking at DM patients and fracture risk with anti-resorptive treatment

• Post-hoc analysis of FIT (Keegan)
  • 3 years of alendronate treatment in women with T2 DM vs. placebo
    • Increased BMD at all sites – 6.6% at LS and 2.4% at the hip
      • Similar change as in non-DM patients
    • Placebo showed a decreased BMD

Leslie. JBMR. 2012
Bisphosphonates & DM

- Antiresorptive drug users (n=103,562) vs age- and sex-matched controls (n=310,683)

Table 3 Risk of various fractures in patients exposed to drugs against osteoporosis vs. nonexposed patients

<table>
<thead>
<tr>
<th>Fracture type/drug</th>
<th>No diabetes</th>
<th>Diabetes</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alendronate</td>
<td>1.85 (1.68–2.04)*</td>
<td>1.97 (1.31–2.95)*</td>
<td>0.77</td>
</tr>
<tr>
<td>Clodronate</td>
<td>4.01 (2.16–7.41)*</td>
<td>2.57 (0.16–42.3)</td>
<td>0.76</td>
</tr>
<tr>
<td>Etidronate</td>
<td>2.07 (1.96–2.19)*</td>
<td>1.80 (1.37–2.36)*</td>
<td>0.32</td>
</tr>
<tr>
<td>Raloxifene</td>
<td>2.19 (1.58–3.02)*</td>
<td>2.27 (0.59–8.70)</td>
<td>0.96</td>
</tr>
</tbody>
</table>

Vestergaard P: Calcif Tissue Int 2011; 88:209
Teriparatide & DM

- DM is a state of low bone formation
  - Therefore, using a bone formation medication would be logical

- Schwartz et al.
  - DANCE study – observational study of men and women with OP treated with teriparatide
  - Post-hoc analysis comparing the effects of teriparatide in pts with T2 DM vs. no DM
    - No difference between groups in non-vertebral fractures and BMD at the total hip and spine
    - Greater increase in BMD at the femoral neck in individuals with DM

Case Resolution

Case 1:

Questions to consider:

• Should this patient be screened for OP with a BMD?
  • Yes, > 50 y.o. age

• Do any elements of this patients history put him at increased risk of fracture?
  • DM prior to puberty
  • Neuropathy – higher risk of falling
  • Could have other AI conditions that put him at higher risk for bone disease (ie. Celiac)
Case Resolution

Case 2

Questions to consider:

• Would you expect her BMD to be low, normal, or high?
  • Normal/High

• Do any elements of this patients history put her at increased risk of fracture?
  • Poor glycemic control
  • Canagliflozin
Take Home Points:

1. Patients with T1 and T2 DM are at increased risk of fragility fracture
   - In excess of risk determined by BMD

2. The mechanism for increased fracture risk is multifactorial

3. New imaging modalities the may be helpful in determining fracture risk

4. Poor glycemic control is linked with increased fracture risk
   - Suggestion: aim for A1C < 8%, while avoiding lows

5. DM medications can have an impact on bone health

6. Prevention and treatment of osteoporosis does not differ in the DM and non-DM population
   - Anti-resorptives appear to be equally effective in DM
Questions?

• Thanks for listening