Treatment Monitoring

Jennifer J. Kelly, DO, CCD, FACE
Associate Professor of Medicine
Associate Chief, Division of Endocrinology and Diabetes
Director of the Metabolic Bone Program
University of Vermont Medical Center
Burlington, VT
Introduction to ZOOM for ECHO

• Please mute microphone when not speaking
• Please use camera as much as possible
• Test both audio & video before joining
• Communicate clearly during session:
  • Can use “raise hand” feature to comment
  • Speak clearly
  • Use chat function for technical issues
• Didactic session will be recorded and shared following the session
CME Disclosures

• University of Vermont (UVM) Office of Continuing Medical and Interprofessional Education (CMIE) is approved as a provider of Continuing Medical Education (CME) by the ACCME.

• UVM designates this educational activity for a maximum of 1.0 AMA PRA Category 1 Credits. Participants should claim only the credit commensurate with the extent of their participation in the activity.

• As an organization accredited by the ACCME to sponsor continuing medical education activities, UVMCMIE is required to disclose any real or apparent conflicts of interest (COI) that any speakers may have related to the content of their presentations.

• Interest Disclosures:
  • None
Objectives

-Determine how monitoring of treatment can be evaluated based on how the diagnosis was made.

-Distinguish between the different parameters that can be assessed.

-Differentiate between how the available medications respond to treatment.
Why was treatment initially started?

- T-score of -2.5 or less
- Fragility fracture
- High FRAX score
Favorable response to treatment

• Improvement over time greater than LSC (least significant change) based on DXA.

• No fractures, however, no treatment guarantees 100% no fractures.

• Bone turnover markers.
Least Significant change

Determined by each machine/site. Preferably by each DXA tech also.

<table>
<thead>
<tr>
<th>Site of Comparison</th>
<th>Least Significant Change (Precision at 95% confidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral Total Hip Mean</td>
<td>0.018</td>
</tr>
<tr>
<td>Total Hip Single Side</td>
<td>0.027</td>
</tr>
<tr>
<td>Bilateral Femoral Neck Mean</td>
<td>0.033</td>
</tr>
<tr>
<td>Femoral Neck Single Side</td>
<td>0.044</td>
</tr>
<tr>
<td>Lumbar Spine L1-L4</td>
<td>0.032</td>
</tr>
<tr>
<td>Lumbar Spine Fewer than 4 Vertebrae</td>
<td>0.037</td>
</tr>
<tr>
<td>Forearm, 1/3 Radius</td>
<td>0.037</td>
</tr>
</tbody>
</table>
DXA monitoring

- Per most guidelines, repeat DXA 1-2 years after starting treatment to assess for response. Can be performed less frequently afterwards.

- Preferably perform at same facility.

- Stable or increasing density with no evidence of new fractures is considered a positive response.
The bone remodelling process

- Osteoclast
- Macrophage
- Osteoblast
- Lining cell
- Osteoid
- New bone
- Osteocytes
- Old bone

Stages:
- Resting
- Resorption
- Reversal
- Formation
- Mineralization
Medications to prevent bone loss and fracture

Bisphosphonates are first line treatment for most people.

Denosumab also works as an anti-resorptive medication.

Anabolic agents build bone.

Important to consider for monitoring treatment and considering bone turnover markers.
Bone turnover markers

CTX is recommended for assessing bone resorption. Should decline with treatment.

PINP is recommended for assessing bone formation or growth. This should increase with anabolic treatments.
Can Treat to Target be used in Osteoporosis?

• Depends on what parameters are being assessed.

• Biggest concern is no fractures, again, no medication guarantees no fractures.

• Favorable DXA response ideal, particularly if considering a drug holiday at some point.
DXA as a surrogate marker

While a person may be responding biologically, they can still have very low BMD and a high risk for fracture.

The goal is to improve the selection of initial drug therapy based on severity, improve follow-up of patients on treatment and anticipate how to use newer treatments that have a very potent effect on BMD and perhaps greater reductions in risk.

Fracture protection should persist with stability. BP response tends to plateau. Unknown if changing to another med to increase BMD will translate into additional anti fracture efficacy.
Recent Fracture

T-score target spoiler: a recent fracture increases future fracture risk regardless. Also many people fracture with normal BMD.

Combination therapy not generally indicated but can be in this situation.

Anabolic agents can help with healing, also used at times with spinal fusions.

Here a goal might be freedom from fractures for 3-5 years.
What to do if a fracture occurs on therapy and/or bone density declines?

• First assess if medication was being taken correctly/regularly if oral.
• Assess for any other underlying secondary cause for bone loss.
• Consider switching or adding on additional treatment if the patient is very high risk for fracture.
• In certain situations waiting to see what happens with next DXA is appropriate.
Issues with Prolia (denosumab)

Some people describe this therapy as indefinite (misleading).

Can be given up to 10 years, should not be stopped abruptly due to effects wearing off and risk for rebound fractures.

Optimal timing of switching to a bisphosphonate remains to be established.

The BP might not be fully incorporated into remodeling sites while remodeling is markedly reduced by denosumab.
Issues with FRAX

For any given value of BMD, fracture risk increases with age.

It is uncommon for someone’s FRAX score to actually increase.

This is not reliable in a person on a drug holiday.

We have limited ability to affect the major risk factors, there are few biomarkers, not enough good data to support a treat-to-target approach.
Role of clinicians

Estimate their patients’ risk

Persuade them that this is a worthwhile strategy.

Based on periodic biomarker or other assessment...

Amend the drug regimen to keep as close to targets as possible.
Summary

• Monitoring response to therapy is important to identify who may require a change in therapy.
• Bone turnover markers not used routinely but can be considered for additional information.
• The finding of a BMD decrease >LSC or a new fracture should trigger an additional evaluation.
• Can consider change in therapy if indicated or closer monitoring
Conclusion

• Volunteers to present cases (this is key to the Project ECHO model)
  • Please submit cases to Jennifer.Kelly@uvmhealth.org

• Please complete evaluation survey after each session

• Claim your CME at www.highmarksce.com/uvmmmed

• Please contact us with any questions, concerns, or suggestions
  Elizabeth.Cote@uvm.edu
  Jennifer.Kelly@uvmhealth.org
Cases/HIPAA

- Names
- Address
- DOB
- Phone/Fax #
- Email address
- Social Security #
- Medical Record #

The discussion and materials included in this conference are confidential and privileged pursuant to 26VSA Section 1441-1443. This material is intended for use in improving patient care.

It is privileged and strictly confidential and is to be used only for the evaluation and improvement of patient care.
Case presentation

RECORDING TO BE STOPPED FOR CASE PRESENTATION