Osteoporosis Guidelines and Hip Fracture.

R. Crilly May 1st, 2013

Guidelines Development

- Old fashioned osteoporosis is a disease of trabecular bone exemplified by spinal compression fractures.
- Can be much reduced by medications, which up to recently were mostly bisphosphonates.
- Also showed these drugs reduce hip fractures.
- So if we can identify those at risk of hip fracture, we can use these drugs to reduce hip fractures.

And wouldn't that be nice as hip fractures are expensive.

- So we moved from thinking of osteoporosis as a disease, to looking at fracture risk, mostly influenced by the risk of non-vertebral fractures.
- These non-vertebral fractures are labeled as fragility fractures.
- Now can assess the risk of fractures using BMD, fracture history etc.
So we assess risk and treat those at high risk.

BUT:
- The drugs are good for trabecular bone deficiency.
- Non-spinal fractures are best predicted by cortical bone measure.
- Question: Is it possible we have been misled and for most people who do not have trabecular bone deficiency but are at increased risk of hip fracture for other reasons the effectiveness of the drugs may be limited.

10-Year Absolute Risk Assessment using Femoral Neck T-score


CAROC Assessment for Women

Prior fragility fracture + steroid therapy puts the patient at high risk of fracture regardless of BMD

CAROC Assessment for Men

Prior fragility fracture or steroid therapy increases fracture risk to the next category.

Hip Fracture is a complex phenomenon.
George Bernard Shaw. Fell out of an apple tree and fractured his hip in his 90s.

“If I survive this I will be immortal”
He didn’t and he wasn’t.


Dementia is a strong risk factor (x3) for hip fracture, which makes the dementia worse.

Pope John Paul II broke his hip in 1994, aged 74. In 1993 he fell and dislocated his shoulder. Had PD, diagnosed in 1993. Perhaps luckier will be the French nun, Angelique Chrisafis, who was cured of her PD after praying to Pope JP in March 2007.

Falls begat falls, co-morbidities important.
Cardinal George of Chicago, age 70, during an Easter service slipped on holy water, landed on the marble floor, and broke his hip. Wore brace on a polio leg and fell frequently.

Prior disability, frequent falls, wet floor, hard surface.

Roger Ebert, hip fracture at age 70.

Weight loss, illness, frailty.

King Haakon of Norway. In 1955, at age 82, fell in his bathroom and broke his. Never walked again. Became depressed over wheelchair existence. Died in 1957

50% of hip fracture patients do not recover their previous level of mobility.
Mrs P. Hip Fracture in an institutionalized demented 92 year old with Trabecular and Cortical Bone Loss.

Hip Fractures are....

- A lot more than just bones.
- Old people fall differently. This is seen in the fracture pattern.

Nature of falling and effect on fractures.

Figure 4-1. Age Specific Incidence Rates for Proximal Femur (Hip), Vertebral (Spine), and Distal Forearm (Wrist) Fractures in Rochester, Minnesota, Men and Women.
Bone and forces placed upon it

Built for loading, not for falling

Falling, a price we pay.

Falling in Young and Old

- Fragility fracture defined as a fracture occurring in a fall from a standing height or less.
- Assumption is that this is what the skeleton should be able to withstand.
- But this may be OK for the young who protect themselves, but not for old who do not.
- So, in old age, you don’t need bad bones to break them.
Vitamin D and Falling

- Issue really is vitamin D and muscle function.
- Long known that there are vitamin D receptors on muscle cells.
- Muscle weakness or myopathy is a part of D deficiency and insufficiency.
- Appears to be important in both trophic (long term) and action (contraction) role.
- In LTC, D levels correlate with falling frequency
- Studies----22% reduction in falling with vit. D.

Fixed structural components.

Length of neck.
Angle of neck.
Proportion of cortical and trabecular bone.

So there are many things that osteoporosis drugs are not going to change
- Falling associated with aging, illness, frailty, etc.
- And the way people fall.
- Structural composition of the hip area.
- Height.
- Weight.
And then…….

- The hip fracture is actually two fractures.

And then, the hip fracture is actually two fractures. Subcapital and intertrochanteric.

Types of Hip Fracture
Is there any evidence we can reduce hip fracture rate?  
Can we prevent the first hip fracture?

Can we prevent the first hip fracture?  
- We can if we can prevent old people falling.  
- Vitamin D will do that. About 20% reduction.  
- What about treating osteoporosis and fracture risk?  
- Will bisphosphonates and other antiresorptives reduce hip fractures?

Original studies done on those with a trabecular bone problem.  
- The absolutely classical diagnostic feature of osteoporosis is the compression fracture. This indicates, not a state of risk, but a disease requiring treatment.
**FIT: Effect of Alendronate on Annual Fracture Incidence in Vertebral Fracture Arm**

- **Spine**: Alendronate (n=1,022) vs. Placebo (n=1,005)
  - p<0.05
- **Multiple Spine**: Alendronate (n=1,022) vs. Placebo (n=1,005)
  - p<0.05
- **Cervical Spine**: Alendronate (n=1,022) vs. Placebo (n=1,005)
  - p<0.05
- **Any Clinical Spine**: Alendronate (n=1,022) vs. Placebo (n=1,005)
  - p<0.05
- **Non-vertebral**: Alendronate (n=1,022) vs. Placebo (n=1,005)
  - p<0.05

**Effect of 3 Years of Treatment With Denosumab on Fractures (All Key Sites) in Women With PMO: FREEDOM**

- **New vertebral**: Placebo (n=3,691) vs. Denosumab (n=3,702)
  - 20% vs. 12%
  - P = 0.0362
- **Nonvertebral**: Placebo (n=3,906) vs. Denosumab (n=3,902)
  - 8% vs. 2%
  - P = 0.0106

**Zoledronic acid 5 mg reduced cumulative 3-year risk of hip fractures by 41%**

- Relative risk reduction vs. placebo: 0.59 (95% CI 0.42-0.83), p=0.002


So, yes, we can reduce hip fracture rate .....
- But it might depend on who you give them to.
- In the studies, they were given to people with low trabecular bone mass, essentially with osteoporosis as we used to know it, that is, spinal fractures.
- Too young?

Hip Fracture Results, Risedronate


So the simple logic....
- We can reduce hip fracture rate
- If we can identify people at risk of hip fracture, then we can prevent some at least.
- May or may not be true because it may depend on whether or not the patient has osteoporosis!
The proof of the pudding..

- Is there any evidence that what we are doing is working?

Population Studies

Does Treatment Change Risk?

- Study of retrospectively calculated fracture risk in 35764 women treated for osteoporosis.
- Divided into high adherers (MPR>80) and low adherers.
- Found only in high risk groups with high adherence was the calculated hip fracture risk reduced. About 8.5%.
  Reduction of about 30-40%, ie about 3% overall.
- Simplest explanation is that it doesn't work for most. Poor targeting is a problem.
- Most likely treated on basis of calculated risk, perhaps with prior fracture influencing the risk level.

Leslie et al 2012 JBMR, 27 (6), 1243-51.
Osteoporosis drug use across Canadian Provinces.

Decline over the decades.


- Conclusion:
  - We can reduce hip fractures in those with osteoporosis.
  - We can't necessarily extend this to those who don't have trabecular bone deficiency.
  - Benefits may accrue only to those selected for low trabecular bone density. This may be only 8% of the ones being currently treated.
After the Hip Fracture……

- What about those who actually break their hip?
- What about preventing the second hip fracture?

Risk of Fracture and Bone Mass; mechanical model

Risk of Fracture and Bone Mass; mechanical model
Fracture Prevalence Across BMD Groups (NORA)

Zoledronic Acid 5 mg Effect on Hip Fractures Over Time

Hazard Ratio, 0.70 (95% CI, 0.41–1.19)  
P = .1815

No. at Risk  
Month

ZOL 5 mg (n = 1065)  
Placebo (n = 1062)

30%NS

NS = not significant

Lyles KW, et al.  

Adapted from Siris ES, et al.  
Conclusion:
- Most people who present with a hip fracture come from the masses at relatively low fracture risk.
- Most may not have the bone problem that responds to treatment.
- Can we identify a sub-group of hip fracture patients that it would be useful to treat?
- Essentially we are asking, who really has osteoporosis?

Presence of Compression Fractures

<table>
<thead>
<tr>
<th>Sub-capital</th>
<th>Inter-trochanteric</th>
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<tbody>
<tr>
<td>Compression (%)</td>
<td>yes</td>
</tr>
<tr>
<td>Percent</td>
<td>100</td>
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| Seem hip and spine (trabecular) density linked.
Spine and Hip Fractures

So for those with a hip fracture
- Make sure the vit.D level is good (over 65nmol/l). Might need 1000-2000IU per day. Both safe.
- Consider those with IT fracture and those with Spinal fracture as likely the true osteoporotic and likely to respond to treatment.
- Treat and follow.

Why is it important to get it right?
- Because of side effects, especially atypical sub-trochanteric fractures of which we are seeing more and more.
Atypical Fractures of the Femoral Diaphysis in Postmenopausal Women Taking Alendronate

Bisphosphonate Stress Fractures

- Fosamax for 11 years.
- No fractures, ever.
- T-score spine -1.7
- T-score femoral neck -0.1.
So......

- We don’t want to treat people with antiresorptives unless sure we are doing some good.
- Choice of treatment is one of the aminobisphosphonates - alendronate (Fosamax), risedronate (Actonel in various forms) zoledronic acid (Aclasta)
- OR denusomab (Prolia).

How do we choose?

- Alendronate is quite long lasting in bones. Might be useful for the very old.
- Risedronate is shorter lasting, but is available as Actonel DR, which can be given with breakfast. Good for institutions.
- Zoledronic acid is once a year infusion, and could possibly be given just after the fracture and will ensure a year’s treatment.
- Denosumab is given by s.c. injection every 6 months. Easy compliance, good for LTC. Might even reduce falling?

Summary
First Hip Fracture Prevention: those with true osteoporosis.
- Make sure those with deficient trabecular bone are treated.
- Identified as those with spinal fractures.
- Height loss, kyphosis etc.
- Evidence supports a significant reduction of hip fracture in these patients on treatment.
- Treat and never stop.

First Hip Fracture Prevention: high risk people.
- 60-year-old woman
- Femoral neck T-score = -2.8
- Based on age and T-score alone = moderate risk
- History of fragility fracture or prolonged systemic glucocorticoid use would shift her to high risk

Treat 5 years and if BMD stable and no further fractures, stop and follow.

Prevent the second hip fracture
- Identify the hip fracture patients with trabecular bone loss.
- The Intertrochanteric fractures is the strong candidate.
- Those with co-existent spinal fractures are strong candidates.
- Those with low spinal BMD are strong candidates (harder to get done).
Mrs P. Hip Fracture in an institutionalized demented 92 year old with Trabecular and Cortical Bone Loss.

Mrs L, 83, fell taking out dog at 3am, never had another fracture. Parkinson’s disease, many falls.

Vitamin D +/- calcium only. Shoot the dog.

END