Osteoporosis, Fracture Risk, and Outcomes in Asians

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Importance of Asian Race in Bone Health

- Between 2000-2010, Asians were the fastest growing subgroup in the US (Census data)
- Asians comprise 5% of the US population and 13% of the California population (2010 Census)
- Asia: 144% projected for population over age 50 where 50% of all hip fractures expected to occur
- Recent data underscore the relevance of Asian race in assessing both fracture risk and outcome

Osteoporosis: A Historical Perspective

- BMD T-score: # SD from young adult BMD mean
- 1994 WHO defined osteoporosis: T-score ≤ -2.5
- 1999/2003 NOF Clinician Guide for treatment:
  - Hip or vertebral fracture
  - T-score ≤ -2.0
  - T-score ≤ -1.5 with clinical risk factors
- 2008 WHO FRAX® Tool to estimate fracture risk
- 2008 Revised NOF Clinician Guide

2. The Asia-Pacific Regional Audit. 2013 (www.iofbonehealth.org)
**Fracture Risk Assessment, FRAX®**

www.sheffield.ac.uk/FRAX/

- US FRAX considers race/ethnicity
  - WHITE
  - BLACK
  - HISPANIC
  - ASIAN

-Reports 10 year probability of major osteoporotic & hip fractures
- Depends on background rates (↓ fracture rates in non-whites) and doesn’t include all risk factors
-Treatment threshold is based on cost effectiveness analysis

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**Fracture Risk Varies by Race & Country**

75 year old 10-yr probability of major osteoporotic fracture (MOF)
No risk factors 10-yr probability of hip fracture (HIP)

<table>
<thead>
<tr>
<th>FRAX® Tool</th>
<th>CRF</th>
<th>T</th>
<th>MOF</th>
<th>HIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>US Caucasian</td>
<td>0</td>
<td>-2.0</td>
<td>13%</td>
<td>3.4%</td>
</tr>
<tr>
<td>US Asian</td>
<td>0</td>
<td>-2.0</td>
<td>7.5%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Japan</td>
<td>0</td>
<td>-2.0</td>
<td>13%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>0</td>
<td>-2.0</td>
<td>11%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Taiwan</td>
<td>0</td>
<td>-2.0</td>
<td>12%</td>
<td>4.2%</td>
</tr>
<tr>
<td>China</td>
<td>0</td>
<td>-2.0</td>
<td>4.9%</td>
<td>1.7%</td>
</tr>
<tr>
<td>India</td>
<td>0</td>
<td>-2.0</td>
<td>7.8%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Philippines</td>
<td>0</td>
<td>-2.0</td>
<td>3.2%</td>
<td>1.0%</td>
</tr>
</tbody>
</table>

*Note: the NOF treatment thresholds are: 20% for MOF, 3% for HIP*

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**Treatment & Fracture Risk Reduction**

<table>
<thead>
<tr>
<th></th>
<th>Hip FX</th>
<th>Vert FX</th>
<th>Non-Vert FX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical first line osteoporosis therapy, cost effective for initial therapy</td>
<td>TREAT</td>
<td>TREAT</td>
<td>TREAT</td>
</tr>
<tr>
<td>Alendronate</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Risedronate</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Alternative initial therapy or when intolerant of oral BP</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Zoledronic acid</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Alternative therapy for high risk patients intolerant of BP or eGFR&lt;30</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Denosumab</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Alternative therapy for severe osteoporosis (anabolic, time-limited use)</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Teriparatide (rPTH)</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Consider for lower risk women with osteoporosis (e.g. younger, no fracture)</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Raloxifene</td>
<td>↓</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
What if Caucasian T changes to Chinese T?

Osteoporosis by BMD & Fracture Risk

- Caucasian T-score is used for US women of all races, based on hip BMD-fracture relationship in white women
- White reference accommodates the higher BMD and lower fracture risk in blacks. How about for Asians?

<table>
<thead>
<tr>
<th>Age</th>
<th>T</th>
<th>MOF</th>
<th>HIP</th>
<th>MOF</th>
<th>HIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>-2.5</td>
<td>12%</td>
<td>1.3%</td>
<td>6.3%</td>
<td>1.2%</td>
</tr>
<tr>
<td>65</td>
<td>-2.5</td>
<td>13%</td>
<td>2.8%</td>
<td>7.3%</td>
<td>1.6%</td>
</tr>
<tr>
<td>70</td>
<td>-2.5</td>
<td>15%</td>
<td>3.9%</td>
<td>8.3%</td>
<td>2.2%</td>
</tr>
<tr>
<td>75</td>
<td>-2.5</td>
<td>17%</td>
<td>5.4%</td>
<td>9.6%</td>
<td>3.1%</td>
</tr>
</tbody>
</table>

NOF Treatment Threshold: 30% 3% 3%

2008 National Quality Metrics (HEDIS)

Women age 67+ fracture: osteoporosis testing or Rx
Women age 65+: osteoporosis testing

Quality goals ensure BMD or treatment in high risk subsets, but do not dictate who should get treated

2008 Guidelines/Metrics: age, BMD, fracture, FRAX

Primary Prevention
- BMD screening at age ≥ 65 (earlier if risk factors)
- Treatment is based on risk (BMD, FRAX™)

Secondary Prevention
- BMD assessment and treatment, risk-based
- HEDIS focus on women age 67+ with fracture

2008 → Increase in Women ≥65 starting BP

2008 National Quality Metrics Revised NOF Guidelines

KP Osteoporosis Program
Hip Fracture Rates increase with Age

![Graph showing the increase in hip fracture rates with age.](image1)

**Huang et al. Osteoporos Int 23:743-750, 2012**

Mortality Following Hip Fracture is High

- 17% mortality ≤ 6 months post-hip fracture
- 23% mortality ≤ 12 months post-hip fracture
  (43% if re-hospitalized within 30 days of discharge)

**Lo et al. Am J Manag Care 21:e206, 2015**

Women with Hip Fracture Odds Ratio* 95% CI

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>0.64</td>
<td>0.51 – 0.80</td>
</tr>
<tr>
<td>Asian</td>
<td>0.75</td>
<td>0.62 – 0.91</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.90</td>
<td>0.70 – 1.16</td>
</tr>
</tbody>
</table>

* Adjusted for age, year, comorbidity index, fracture type, prior fracture

- Asians have 1/3 ↓ 1-year mortality risk post hip fracture
- Whether findings reflect health, social or socioeconomic factors or overall mortality differences by race is unclear
- 1-year post-fracture mortality similar across the 3 largest Asian subgroups (Chinese, Japanese, Filipina women)


Approach to Osteoporosis for US Asians

- FRACTURE
  - Assess BMD & Fracture Risk
    - T ≤ -2.5
      - Treat
    - -2.5 < T < -1.0
      - Treat
    - T ≥ -1.0
      - Screen for Vitamin D deficiency
      - Increase dietary calcium intake

- Major Osteoporotic Fracture
- Hip / Vertebral Fracture

FRAX 10-yr probability
- Hip Fracture (FX)
- Major Osteoporotic FX
- ≥ 3% ≥ 20%
  - Treat
Ensure Adequate Vitamin D Repletion

- 42% of US adults have Vitamin D deficiency (NHANES)
- Vitamin D deficiency in Asians, repletion success lower

<table>
<thead>
<tr>
<th>N = 72,093, with 25OHD &lt; 20 (D3 Rx)</th>
<th>25OHD ≤ 10</th>
<th>25OHD 10-19</th>
<th>Odds of repletion with D3 50,000 IU x 12 wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>31,584</td>
<td>18%</td>
<td>82%  OR 0.8 (0.7-0.9)</td>
</tr>
<tr>
<td>Asian</td>
<td>11,208</td>
<td>17%</td>
<td>83%  OR 0.8 (0.7-0.9)</td>
</tr>
</tbody>
</table>


Optimize Dietary CA Intake in Asians

- Asian diet generally low in dairy, may be low in calcium
- Calcium-rich foods: tofu, broccoli, bok choy, edamame
- If lactose intolerance, suggest lactase supplement

Dietary & Lifestyle Intervention

- Vitamin D supplement
- Dietary Calcium
- Quit smoking
- Limit alcohol
- Optimize weight
- Exercise

PREVENT FALLS

Falls Prevention in Older Adults

- Over 1 in 4 older adults report a fall in past year
- Falls are leading cause of osteoporotic fracture
- Fall Risk and Safety Assessment is a CMS priority

CDC STEADI Program

SCREEN AT AGE 65+
Have you fallen in the past year?
Feel unsteady standing or walking?
Do you worry about falling?
ASSESS & INTERVENE
www.cdc.gov/steadi

2008/2011 KPNC Members Health Survey
1 in 4 women age ≥65 fell in past year

28% 22% 27% 20% 13% 12% 15% 8%

1 or more falls 2 or more falls

Adjusted Odds Ratio (95% CI): Outcome = Falls in Past Year

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>1+ Falls</th>
<th>2+ Falls</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Black</td>
<td>0.73 (0.55 – 0.95)</td>
<td>0.85 (0.59 – 1.23)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.94 (0.71 – 1.24)</td>
<td>1.21 (0.83 – 1.76)</td>
</tr>
<tr>
<td>Asian</td>
<td>0.64 (0.51 – 0.82)</td>
<td>0.62 (0.43 – 0.88)</td>
</tr>
</tbody>
</table>

Geng et al. BMC Geriatrics 2016
Initial and Secondary Lab Evaluation

2° evaluation: 
- TSH
- ALKP
- LFTs
- PTH
- 24h urine calcium
- Ca
- PO4
- 25D
- CBC
- Cr
- 2° evaluation: ± bone markers

Initial and Secondary Lab Evaluation

2° evaluation: 
- SPEP, UPEP
- ? Celiac TTG

2° evaluation: 
- ± bone markers

How Long to Treat with BP?

KPNC women age ≥50 initiating oral BP (2002-2007)

<table>
<thead>
<tr>
<th>N = 48,390</th>
<th>White (65%)</th>
<th>Asian (17%)</th>
<th>All other (17%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70.6 ± 10.2</td>
<td>66.4 ± 8.8</td>
<td>68.9 ± 9.6</td>
</tr>
<tr>
<td>Prior Fracture</td>
<td>29.1%</td>
<td>12.9%</td>
<td>22.9%</td>
</tr>
<tr>
<td>BP duration (years)</td>
<td>2.7 (0.7-5.2)</td>
<td>3.8 (1.2-6.1)</td>
<td>2.4 (0.7-5.0)</td>
</tr>
</tbody>
</table>

Lo et al. Bone 85:142-147, 2016

Practice Guidelines

- After 3-5 years BP treatment
- Obtain follow-up BMD
- Review fracture history & fracture risk
- Consider BP holiday
- Osteopenia
- Low fracture risk
- No fracture
- No hip or spine fracture
- No multiple fractures

Consider BP continuation
- Hip or spine FX
- Multiple OP FX
- T ≤ -3.5, no FX
- FN T ≤ -2.5
- High FRAX
- Age >70-75 yrs

Femur Fracture in Women by Age

<table>
<thead>
<tr>
<th>AGE ≥ 50 years</th>
<th>AGE 50 – 79 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIP</td>
<td></td>
</tr>
<tr>
<td>WHITE</td>
<td></td>
</tr>
<tr>
<td>FRAC</td>
<td></td>
</tr>
<tr>
<td>Diaphyseal</td>
<td></td>
</tr>
<tr>
<td>Diaphyseal FX and ↑ BP use, esp in Asians</td>
<td></td>
</tr>
</tbody>
</table>

UpToDate FLEX Study findings Adler et al. J Bone Miner Res 31:16-35, 2016

### Risk of Atypical Femur Fracture (AFF)

- 48,390 women (median BP 2.8 yrs, over 7.7 yrs follow-up)
- 68 AFF (0.14%), median BP 5.5 yrs (IQR 4.2-7.0)
- AFF cases: 60% Asian (majority Filipina and Chinese)
- AFF incidence 18.7 per 100,000 person yrs follow-up

<table>
<thead>
<tr>
<th>Race</th>
<th>AFF Incidence</th>
<th>Adjusted Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>7.6 per 100,000 yrs</td>
<td>- -</td>
</tr>
<tr>
<td>Asian</td>
<td>64.2 per 100,000 yrs</td>
<td>6.6 (3.7 - 11.5)</td>
</tr>
<tr>
<td>All Others</td>
<td>14.3 per 100,000 yrs</td>
<td>2.1 (0.9 - 4.6)</td>
</tr>
</tbody>
</table>

- Incidence of AFF is extremely low, but 6x higher in Asians
- Does AFF with long term BP favor BP holiday in Asians?

Lo et al. Bone 85:142-147, 2016

### SUMMARY

- Osteoporosis is prevalent among US Asians
- Increase BMD screening, risk assessment, treatment

**Fracture prevention:** Focus on modifiable factors
- Prevent Falls: safety assessment, intervention, exercise
- Dietary Ca 1200 mg, Vit D 1000 IU, screen 25OHD level

**Pharmacologic treatment:** Fracture risk reduction
- Initial BP treatment period: Benefits far outweigh risks
- After 3-5 years BP: Reassess: Consider BP holiday?
- Future studies should address: Optimal BP duration? Racial differences in risk – benefit ratio after 5 years?

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  - National Institute of Aging
  - National Institute of Arthritis, Musculoskeletal Disorders and Skin Diseases