BONE FRACTURE

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OUTLINE

CHIP fracture
• Poor survival
• GP and Dialysis pts
• Regional variation
• Dialysis modality
• Trend

Vertebral fracture

CHRONIC KIDNEY DISEASE MINERAL AND BONE DISORDER

LABORATORY ABNORMALITIES

CVD
Fractures
MORTALITY

BONE ABNORMALITIES

VASCULAR CALCIFICATION

CKD-MBD
Hip fracture

- subtrochanteric fx
- head fx
- neck fx
- basi-cervical fx, basal fx
- trochanteric fx & intertrochanteric fx
- subtrochanteric fx

5cm
HIP FRACTURE IS ASSOCIATED WITH POOR OUTCOME IN THE GENERAL POPULATION


HIP FRACTURE IS ASSOCIATED WITH POOR OUTCOME AMONG DIALYSIS PATIENTS


A matched cohort study of dialysis patients using data from the USRDS

KDIGO
HIP FRACTURE IS ASSOCIATED WITH POOR OUTCOME


A matched cohort study of dialysis patients using data from the USRDS

No fracture/No CVD
No fracture/CVD
Fracture/No CVD
Fracture/CVD
Dialysis patients have more risks of hip fracture compared with the general population.

**General population**
Older age, female gender, low BMI, low BMD, early menopause, smoking, physical activity levels, etc.

**Dialysis patients**
A beta-2M-amyloidosis and related osteopathy, CKD-MBD, dialysis modality, etc.

**Common risk factors**

**Dialysis patient-specific factors**
HIP FRACTURE INCIDENCE AMONG DIALYSIS PATIENTS WAS 4 TIMES HIGHER THAN THAT OF THE GENERAL POPULATION.

This study included only Caucasians.

How about Asians?

DIALYSIS PATIENTS HAVE DEFINITELY HIGHER RISK OF HIP FRACTURE COMPARED WITH THE GENERAL POPULATION


INCIDENCE: 11.3/1,000 PATIENT-YEARS
(95% CI, 10.7 TO 11.9)

General population

Hip fracture incidence among Japanese general population

JRDR: the Japanese Society for Dialysis Therapy Registry

5-6 times

HD patients

Hip fracture incidence among Japanese HD patients
THE OVERALL INCIDENCE OF HIP FRACTURE AMONG JAPANESE HD PTS WAS 5- TO 6-FOLD GREATER THAN IN THE GENERAL POPULATION.

**Standardized Incidence Ratio**

**Men**

6.2 (95%CI 5.7 - 6.8)

**Women**

4.9 (95%CI 4.6 - 5.3)

SIRS are already high in pts w/ short dialysis

VINTAGE

<table>
<thead>
<tr>
<th>Vintage, years</th>
<th>Mean age (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 1</td>
<td>64.8 (12.7)</td>
</tr>
<tr>
<td>1</td>
<td>64.9 (12.6)</td>
</tr>
<tr>
<td>2 to 3</td>
<td>64.8 (12.5)</td>
</tr>
<tr>
<td>4 to 7</td>
<td>64.3 (12.3)</td>
</tr>
<tr>
<td>8 to 15</td>
<td>62.1 (12.1)</td>
</tr>
<tr>
<td>More than 16</td>
<td>59.5 (10.1)</td>
</tr>
<tr>
<td></td>
<td>67.6 (12.7)</td>
</tr>
<tr>
<td></td>
<td>67.2 (13.2)</td>
</tr>
<tr>
<td></td>
<td>67.4 (12.8)</td>
</tr>
<tr>
<td></td>
<td>66.0 (12.7)</td>
</tr>
<tr>
<td></td>
<td>63.5 (12.1)</td>
</tr>
<tr>
<td></td>
<td>61.5</td>
</tr>
</tbody>
</table>

Error bars indicate 95% confidence intervals.

The country-specific rate for hip fracture in the dialysis population is higher than reported rates for hip fracture in the general population.

Dialysis patients face higher risks for hip fracture compared to the general population.
TAIWAN NATIONAL COHORT STUDY
1903 PATIENTS HAD A HIP FRACTURE (INCIDENCE: 89.21/10,000)

1903/Patient time at risk = 89.21/10,000

Patient time at risk = 213316.9

95% CI
= 85.2 to 93.3/10,000
The question arises why hip fracture incidence varies so much.

Tentori F et al. *Kidney Int* 2014

Wakasugi M et al. *JBMM* 2013

Lin ZZ et al. *Bone* 2014

Japanese Society for Dialysis Therapy Registry (JRDR)

Taiwan National Cohort Study
The question arises why hip fracture incidence varies so much.

The reasons are not known.

**General population**

- Common risk factors: Older age, female gender, low BMI, low BMD, early menopause, smoking, physical activity levels, etc.

**Dialysis patients**

- Dialysis patient-specific factors: A beta-2M-amyloidosis and related osteopathy, CKD-MBD, dialysis modality, etc.
LARGE VARIATIONS IN FRACTURE INCIDENCE EXIST IN THE GENERAL POPULATION

Common risk factors
Older age, female gender, low BMI, low BMD, early menopause, smoking, physical activity levels, etc.
AGE-STANDARDIZED INCIDENCE RATES OF HIP FRACTURE VARIES ABOUT 10-FOLD IN THE GENERAL POPULATION

Hip fracture rates for men and women combined in different countries of the world categorised by risk.

Where estimates are available, countries are colour coded red (annual incidence >250/100,000), orange (150-250/100,000) or green (<150/100,000)

Hip fracture incidence among Asians are approximately half that of Caucasians for both sexes.

Yamamoto K et al. Osteoporosis Int (1993) Suppl. 1:S48-50

Why Asians have lower incidence of hip fracture compared to Caucasians?

Asians have a bone density similar to or lower than that of Caucasians.

Fig. 1. Age-specific incidence of proximal femoral fractures in women in different countries.

Yamamoto K et al. Osteoporosis Int (1993) Suppl. 1:S48-50
The reasons why Asians have lower incidence of hip fracture compared to Caucasians are not well understood.

Some traditional lifestyle characteristics may prevent hip fracture.

- **Tatami** (traditional Japanese mat)
- **Futon** bedding

The custom of living and sleeping on the floor on a tatami, and using futon bedding.

- **Japanese green tea**
- **Natto** fermented soybeans rich in vitamin K₂ (menaquinone-7)
- **Tofu** soy products containing a high amount of isoflavones

Short legs


Yamamoto K et al. *Osteoporosis Int* 1993;Suppl. 1:S48-50.
In addition to large variations in fracture rates around the world,

Hip fracture rates for men and women combined in different countries of the world categorised by risk.

Where estimates are available, countries are colour coded red (annual incidence >250/100,000), orange (150-250/100,000) or green (<150/100,000).

Hip fracture rates vary within countries

Japanese general population

**Men**

- **western Japan**
  - Standardized incidence ratio (SIR): 1.20~
  - 1.10~1.19
  - 1.00~1.09
  - 0.90~0.99
  - ~0.89

**eastern Japan**

- Standardized incidence ratio (SIR): 1.20~
- 1.10~1.19
- 1.00~1.09
- 0.90~0.99
- ~0.89

**Women**

- **western Japan**
  - Standardized incidence ratio (SIR): 1.20~
  - 1.10~1.19
  - 1.00~1.09
  - 0.90~0.99
  - ~0.89

- **eastern Japan**
  - Standardized incidence ratio (SIR): 1.20~
  - 1.10~1.19
  - 1.00~1.09
  - 0.90~0.99
  - ~0.89

Hip fracture incidence is higher in western Japan than in eastern Japan.

HIP FRACTURE RATES VARY WITHIN COUNTRIES

JAPANESE HD PATIENTS


Standardized incidence ratio (SIR)

- 1.4 ≤ 1.20 - 1.39
- 1.00 - 1.19
- 0.90 - 1.09
- 0.70 - 0.89
- 0.50 - 0.69
- ≤ 0.49

Hip fracture incidence is higher in western Japan than in eastern Japan.
The question arises why hip fracture incidence varies so much. The reasons are not known.

Common risk factors
Older age, female gender, low BMI, low BMD, early menopause, smoking, physical activity levels, etc.

Dialysis patient-specific factors
A beta-2M-amyloidosis and related osteopathy, CKD-MBD, dialysis modality, etc.
UNADJUSTED TEMPORAL TREND IN INCIDENCE OF HIP FRACTURES OVER TIME: HD COMPARED TO PD

CUMULATIVE INCIDENCE OF HIP FRACTURE AFTER BEGINNING DIALYSIS STRATIFIED BY DIALYSIS MODALITY


Table 2
Risk factor for hip fracture in patients with end-stage renal disease and on dialysis (n = 51,473).

<table>
<thead>
<tr>
<th>Factors</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>Sex (female v male)</td>
<td>1.343 (1.225–1.473)✉</td>
<td>1.256 (1.143–1.380)✉</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–44</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>45–64</td>
<td>5.159 (3.820–6.967)✉</td>
<td>4.269 (3.154–5.780)✉</td>
</tr>
<tr>
<td>Dialysis modality (HD v PD)</td>
<td>2.269 (1.755–2.934)✉</td>
<td>1.311 (1.012–1.698)✉</td>
</tr>
<tr>
<td>Prior transplantation (yes v no)</td>
<td>0.300 (0.113–0.801)</td>
<td>1.094 (0.408–2.930)</td>
</tr>
<tr>
<td>Prior hip fracture (yes v no)</td>
<td>2.718 (2.182–3.385)✉</td>
<td>1.438 (1.140–1.798)✉</td>
</tr>
<tr>
<td>Osteoporosis (yes v no)</td>
<td>1.894 (1.633–2.197)✉</td>
<td>1.242 (1.066–1.448)✉</td>
</tr>
<tr>
<td>Diabetic Mellitus (yes v no)</td>
<td>2.001 (1.825–2.193)✉</td>
<td>1.662 (1.511–1.828)✉</td>
</tr>
<tr>
<td>Congestive heart failure (yes v no)</td>
<td>1.532 (1.386–1.694)✉</td>
<td>1.099 (0.992–1.218)</td>
</tr>
<tr>
<td>Cerebrovascular disease (yes v no)</td>
<td>1.654 (1.455–1.879)✉</td>
<td>1.149 (0.804–1.642)</td>
</tr>
<tr>
<td>Liver cirrhosis (yes v no)</td>
<td>1.276 (1.067–1.526)✉</td>
<td>1.374 (1.149–1.644)✉</td>
</tr>
<tr>
<td>Psychiatric disorder (yes v no)</td>
<td>1.240 (0.865–1.779)</td>
<td>1.201 (0.837–1.725)</td>
</tr>
<tr>
<td>Dementia (yes v no)</td>
<td>1.617 (0.868–3.012)</td>
<td>0.853 (0.457–1.593)</td>
</tr>
</tbody>
</table>

HR, hazard ratio; CI, confidence interval; HD, hemodialysis; PD, peritoneal dialysis.

* HR adjusted for sex, age, dialysis modalities, prior transplantation, prior hip fracture, osteoporosis, diabetes mellitus, congestive heart failure, cerebrovascular accident, liver cirrhosis, psychiatric disorder and dementia.

p < 0.05.
**Patients on PD had about 30% lower risk of hip fracture than did those on HD**

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>0.64 (95% CI 0.49 – 0.81)</td>
<td>0.69 (95% CI 0.55 – 0.85)</td>
</tr>
<tr>
<td>40-49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-59</td>
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<tr>
<td>60-69</td>
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<tr>
<td>70-79</td>
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<tr>
<td>80-89</td>
<td></td>
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<tr>
<td>≥90</td>
<td></td>
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</tr>
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Error bars indicate 95% confidence intervals.

Figure 11.12 Percentage distribution of type of renal replacement therapy modality used by ESRD patients, by country, in 2015.

The USRDS 2017 Annual Data Report
Incidence rates for hip fracture have declined since 2005 among incident dialysis patients in the US.

TRENDS ARE DIFFERENT BETWEEN THE GENERAL NON-ESRD POPULATION AND HD PATIENTS

The improved trend in the hemodialysis pts is suggested to be due to factors specific to hemodialysis pts.

AGE-STANDARDIZED HIP FRACTURE INCIDENCE IN JAPAN HAVE DECLINED IN FEMALE AND SHOWED NO CHANGE IN MALE DIALYSIS PATIENTS

Open and filled circles represent the crude and age-standardized rates, respectively. The reference population was the 2013 population of Japanese dialysis patients. Lines are fitted rates based on joinpoint analysis.

Japanese general population has a continuing increase in age-adjusted rates of hip fracture.

EVIDENCE-BASED GUIDELINES AND THE CONCEPT OF CKD-MBD MAY CONTRIBUTE TO THE IMPROVEMENTS

The JSDT clinical practice guidelines for management of secondary hyperparathyroidism in maintenance dialysis patients was published in 2006. This is the first clinical guidelines to be published after the clinical concept of CKD-MBD was introduced by KDIGO.

THE TARGET RANGE FOR INTACT PTH IS MUCH LOWER THAN THOSE FROM OTHER COUNTRIES

The JSDT clinical practice guidelines for management of secondary hyperparathyroidism in maintenance dialysis patients was published in 2006.

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<tr>
<td>Intact PTH</td>
<td>60-180 pg/mL</td>
<td>60-240 pg/mL</td>
</tr>
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</table>

POSTMENOPAUSAL FEMALE DIALYSIS PATIENTS HAVE MORE BONE LOSS THAN MALE DIALYSIS PATIENTS WITH COMPARABLE PTH CONCENTRATIONS


Concentrations of serum bone resorption markers are significantly higher in postmenopausal female hemodialysis patients compared with males with similar serum PTH concentrations.
THE TARGET RANGE IN JAPAN MAY BE FAVORABLE FOR FEMALE BONES


Target range for dialysis patients

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KDIGO
The improved trend in the dialysis patient is likely due to factors specific to dialysis patients.

The approval of cinacalcet in March 2004

The approval of cinacalcet in 2008

The approval of cinacalcet in 2008


**SUMMARY**

**General population**

Common risk factors
- Older age
- Female gender
- Low BMI
- Low BMD
- Early menopause
- Smoking
- Low physical activity levels

**Dialysis patients**

Dialysis patient-specific factors
- A beta-2M-amyloidosis and related osteopathy
- CKD-MBD
- Dialysis modality

**Poor outcome**

Hip fracture

**Kanis JA, et al. Osteoporos Int 2012; 23(9):2239–56.**

**KDIGO**

THE QUESTION ARISES WHY HIP FRACTURE INCIDENCE VARIES SO MUCH
THE REASONS ARE NOT KNOWN
AGE-SPECIFIC INCIDENCE RATES IN HONG KONG COMPARED TO JAPANESE AND SWEDISH CAUCASIANS FOR HIP FRACTURE


[Graph showing incidence rates for men and women in different age groups for Hong Kong, Japan, and Sweden.]

KDIGO
AGE-SPECIFIC INCIDENCE RATES IN HONG KONG COMPARED TO JAPANESE AND SWEDISH CAUCASIANS FOR CLINICAL VERTEBRAL FRACTURE

OUTLINE

Hip fracture
• Poor survival
• GP and Dialysis pts
• Regional variation
• Dialysis modality
• Trend

Vertebral fracture

CHRONIC KIDNEY DISEASE
MINERAL AND BONE DISORDER

LABORATORY ABNORMALITIES

BONE ABNORMALITIES

CVD
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CKD-MBD