CVD in CKD: Asian Experience

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Dialysis Unit, University Hospital of The Ryukyus, Okinawa, Japan
Contents of the Presentation

1. General Japanese population
   Prevalence of “lifestyle related disease”
   Trends of BMI & proteinuria among screened subjects
   Studies on CKD vs. CVD
     eGFR, proteinuria, and underlying kidney disease

2. ESRD population: demographics
   The Japanese Society for Dialysis Therapy (JSDT) registry
   Underlying kidney disease, age, gender
   Causes of death: GP vs. ESRD

3. Factors related to increased mortality risk among ESRD patients
   Pre-HD blood pressure & pulse rate
   RAS vs. non-RAS drugs
   Treatment of hypertension: ongoing RCT

4. Asian Forum of CKD Initiative (ACKDI)
   Pan Asian CKD registry
   Rapid increase in ESRD patients in China
### Lifestyle related disease

<table>
<thead>
<tr>
<th>Condition</th>
<th>Rate</th>
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<tbody>
<tr>
<td>Hypertension</td>
<td>3,500</td>
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<tr>
<td>DM</td>
<td>740</td>
</tr>
<tr>
<td>Pre-DM</td>
<td>880</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>600</td>
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<td>Obesity</td>
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</tr>
<tr>
<td>Hyperuricemia</td>
<td>500</td>
</tr>
<tr>
<td>Gout</td>
<td>30〜50</td>
</tr>
<tr>
<td>CKD</td>
<td>1,330</td>
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</tbody>
</table>

X10,000

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Japanese eGFR formula

Prevalence of Proteinuria

![Graph showing the prevalence of proteinuria by age and gender.](image-url)
CKD Prevalence: Hisayama Study


**CKD stage 3-5**
*P<0.01 vs. 1974
Age≥40, age-adjusted
Men

Log-Rank
p<0.01

CKD (+)
35.6% in 12yrs

Women

Log-Rank
p<0.01

CKD (+)
22.0% in 12yrs

Cumulative rate, %

RR

CVD IHD CI CH

1.0
1.0
1.0
1.0

1.4
1.9
1.2
0.7

* p<0.05 vs. CKD (-)

N=2,634, 1988-2000, adjusted

† age, sex, hypertension, ECG, DM, BMI, TC, TG, HDL-C, homocysteine, hs-CRP, smoking, alcohol


CKD vs CVD : Hisayama study

CKD (+) = GFR < 60 ml/min/1.73m²

N=2,634, 1988-2000, not-adjusted

0 2 4 6 8 10 12 yrs

0 10 20 30 40 50
CKD vs CVD: Okinawa

Cumulative Incidence of Cardiovascular Disease or ESRD, per 1,000 patient during the study period

Age  <60  ≥60  <60  ≥60
Chronic kidney disease  -  -  +  +
Number of screenees 6,108 398 3,382 4,095

Iseki K et al. Vasc Dis Prev 3;327-333, 2006
CVD deaths are related with proteinuria and low eGFR

Life style in “Edo” period
Different Clinical outcomes for CVD
The Gonryo study

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio (95% CI)</th>
<th>CVD</th>
<th>Death</th>
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<tbody>
<tr>
<td>Primary CKD</td>
<td>1.00</td>
<td>10</td>
<td>4</td>
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<tr>
<td>Hypertension</td>
<td>2.87 (1.37-6.02)</td>
<td>20</td>
<td>5</td>
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<tr>
<td>Diabetes Mellitus</td>
<td>11.88 (4.58-30.83)</td>
<td>26</td>
<td>7</td>
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<tr>
<td>Other CKD</td>
<td>3.59 (1.81-7.09)</td>
<td>13</td>
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</table>

N=2,692 CKD patients, 1-yr cohort study
Adjusted for age, gender, Hb, proteinuria, SBP, BMI, hyperlipidemia, DM, steroid, smoking, history of CVD

ESRD 113, CVD 69, death 24, lost F/U 200

Natural Course to Dialysis: Markov model

- **C3** CKD (Early detection & treatment)
- **C4** CKD (Symptomatic)
- **C8** Intervention
- **C5** ESRD
- **Death**

Ischemic Events +/-

The Japanese Society of Nephrology (JSN) Task Force for the Validation of Urine Examination as an Universal Screening (VALUE-US)
Prevalence of Hypertension

Nationwide Specific Health Check and Guidance System in Japan, N=332,174
Prevalence of CVD History

Nationwide Specific Health Check and Guidance System in Japan, N=332,174
Incidence by renal disease : ESRD

Mean age:
- CGN: 60.5, 66.4, 66.9
- DM: 62.5, 65.4, 65.6
- NScl: 71.4, 73.7, 74.0

Number of patients:
- CGN: 12,000, 16,000
- DM: 18,000
- NScl: 10,000

Year:

JSDT
Mean Age of Patients : ESRD

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<th>Incident</th>
<th>Prevalent</th>
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Incidence by gender: ESRD

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Causes of Death in Prevalent Patients

- Cardiac: 20%, 25%, 30%, 35%, 40%
- Stroke: 0%, 5%, 10%, 15%, 20%
- Malignancies: 15%, 10%, 11%, 12%, 13%
- Infection: 25%, 30%, 35%, 40%
- Acute myocardial infarction: 5%, 6%, 7%, 8%, 9%

Annual Mortality rate

- Men
- Women
- ESRD Patients
- General Population

Mortality rate vs. Age, years

JSDT, MHWL
Prognosis: ESRD pts vs. CVD pts

Survival over time for different conditions:
- GP: acute MI
- GP: stroke
- ESRD

Observation, months

Survival of Dialysis Patients

JSĐT database
1. Pre-HD blood pressure (N=163,668)
2. Pre-HD pulse rate (N=147,702)

Prevalent patients cohort
* Mean Age 63.6 yrs, DM 31.4%, BMI 21.1
* Mean Vintage 8.0yrs (more than 10,000 pts; >25 yrs)
* History of CVD
  AMI 6.1%
  CH 3.7%
  CI 11.8%
  Amputation 2.4%
Pre-HD systolic BP vs. Survival

Adjusted odds ratio (95% CI)

Anti-hypertensive drugs
- none
- yes

Pre-HD systolic BP, mmHg
- <100
- 100-
- 120-
- 140-
- 160-
- 180-
- 200-

Iseki K et al. Nephron Clinical practice 113; C183-C190, 2009
Pre-HD diastolic BP vs. Survival

Anti-hypertensive drugs
- none
- yes

Adjusted odds ratio (95% CI)

Pre-HD diastolic BP, mmHg
- <60
- 60-70
- 80-90
- 90-100
- 100-110

Iseki K et al. *Nephron Clinical practice* 113; C183-C190, 2009
Effects of drug treatment

Iseki K et al. *Nephron Clinical Practice* 113; C183-C190, 2009
Distribution of Pulse Rate

Number of Patients

Pre-HD Pulse Rate, bmp

Iseki K et al. NDT2010, in press
Pulse Rate and Survival

Iseki K et al. NDT2010, in press
Olmesartan Clinical Trial in Okinawan Patients Under OKIDS

Cochran Renal Group
www.cochran-renal.org
CRG010600030

Iseki K et al. Clin Exp Nephrol 13; 145-151, 2009
Protocol

Follow-up (3 yrs)

Hypertension

screening

>1 month

Non RAS inhibitors

DW control

Olmesartan

RAS inhibitors

DW control

Events

Death, CVD

Baseline data

- Exclusion & inclusion criteria
- Informed & written consent
- Randomized by sex & DM

End of follow-up

- Safety
Prevalent HD Patients in Okinawa 2005  
N=3,529

Preliminary Screening at Contracted Units
N=1,240  
RAS (-) : N=640  
RAS (+) : N=600

Informed Consent  
N=533

Excluded  
1. Not signed  (N=49)  
2. Against inclusion criteria  (N=15)

Randomization  
2006 June to 2008 June  
N=469

Target BP  
<140/90mmHg at Pre-HD

Follow-up by 2011 June
### Blood pressure: Pre-HD vs. Home

<table>
<thead>
<tr>
<th></th>
<th>Total (N=210)</th>
<th>RAS (+) (N=107)</th>
<th>RAS (-) (N=103)</th>
<th>P value</th>
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<td><strong>Pre-HD</strong></td>
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<tr>
<td>Systolic BP, mm Hg</td>
<td>158.8 (814.4)</td>
<td>157.5 (15.1)</td>
<td>160.1 (13.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>81.2 (10.7)</td>
<td>81.3 (10.1)</td>
<td>81.2 (11.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Pulse rate, bpm</td>
<td>77.4 (9.8)</td>
<td>77.8 (10.3)</td>
<td>77.5 (9.3)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Home</strong></td>
<td></td>
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</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>150.5 (16.6)#</td>
<td>150.9 (16.1)*</td>
<td>150.0 (17.1)#</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>84.1 (11.3)#</td>
<td>84.6 (10.5)*</td>
<td>84.0 (12.0)*</td>
<td>NS</td>
</tr>
<tr>
<td>Pulse rate, bpm</td>
<td>74.9 (10.6)*</td>
<td>75.7 (11.6)</td>
<td>73.8 (9.3)*</td>
<td>NS</td>
</tr>
</tbody>
</table>

#P<0.0001, *P<0.005
WG 2, Pan Asian CKD Registry

Co-chairs: Kunitoshi Iseki, Vivekanand Jha
Members: Evan Lee, Jafar H Tazeen, Lynn A Gomez, Randal Faull, Zaki Morad, T Criang, Chin Ho Jun, Toshiaki Monkawa, Vlado Perkovic
Aim of the Pan Asian Registry

To provide concrete data of CKD registry on prevalence, incidence based on the sources, collecting method (proteinuria, Albuminuria, eGFR)

- regional difference
- set-up outcome variables
- find unique problems in Asian countries
Questions addressed with the registry

- What are the key outcomes of CKD?
  Risk of CVD and mortality with CKD;
    
  *may be different among Asians*

  Prevalence of IgA GN;
  
  *vary by ethnic background and geographical area*
Rapid increase in ESRD in China

- Total number on maintenance dialysis:
  - 41,755 (1999)
  - 65,074 (2007)
  - 120,000 (2009, not complete yet)

- Prevalence of ESRD, per million population
  - 33.2 (1999)
  - 51.7 (2008)
  - 92.3 (2009, 1.3 billion)

Within 5 years, N of ESRD becomes larger than JSDT!
Summary of the presentation

**CKD and CVD:**
*Asians vs. non-Asian countries*

**Similarities**
- Increasing prevalence of CKD & ESRD
- CKD as a risk factor of CVD

**Dissimilarity**
Effect of gender, obesity, and underlying kidney disease
- More ESRD than CVD
- Better survival of ESRD patients in Japan