CKD Asia – What’s Common and What’s Different from the West?

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CHRONIC KIDNEY DISEASE MINERAL AND BONE DISORDER

Biomarkers?

CKD-MBD

BMD
Bone Biopsy

KDIGO

Laboratory Abnormalities
Bone Abnormalities
CVD Abnormalities
Fractures
Mortality
Vascular Calcification

Kidney Int 76 (Suppl 113):S1-S130, 2009
KEY MESSAGES

• Prospective studies evaluating BMD testing in adults with CKD represent a substantial advance since the original guideline from 2009, making a reasonable case for BMD testing if the results will impact future treatment.

• It is important to emphasize the interdependency of serum calcium, phosphate, and PTH for clinical therapeutic decision-making.

• Phosphate-lowering therapies may only be indicated in the case of “progressive or persistent hyperphosphatemia”.

• New evidence suggests that excess exposure to exogenous calcium in adults may be harmful in all severities of CKD, regardless of other risk markers.
KEY MESSAGES

• It is reasonable to limit dietary phosphate intake, when considering all sources of dietary phosphate (including “hidden” sources).

• The **PRIMO** and **OPERA** studies failed to demonstrate improvements in clinically relevant outcomes but did demonstrate increased risk of hypercalcemia. Accordingly, routine use of calcitriol or its analogs in CKD G3a-G5 is no longer recommended.

• No consensus was reached to recommend cinacalcet as first-line therapy for lowering PTH in all patients with SHPT and CKD G5D.
# High ESRD Incidence in Asia

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence, pmp</th>
<th>%DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taiwan</td>
<td>476</td>
<td>45%</td>
</tr>
<tr>
<td>Brunei</td>
<td>393</td>
<td>NA</td>
</tr>
<tr>
<td>Thailand</td>
<td>338</td>
<td>40%</td>
</tr>
<tr>
<td>Singapore</td>
<td>319</td>
<td>66%</td>
</tr>
<tr>
<td>Japan</td>
<td>290</td>
<td>44%</td>
</tr>
<tr>
<td>Rep. of Korea</td>
<td>285</td>
<td>48%</td>
</tr>
<tr>
<td>Malaysia</td>
<td>261</td>
<td>64%</td>
</tr>
<tr>
<td>Jalisco (Mexico)</td>
<td>411</td>
<td>62%</td>
</tr>
<tr>
<td>USA</td>
<td>378</td>
<td>45%</td>
</tr>
</tbody>
</table>

China? India?
BETTER SURVIVAL IN JAPAN: WHY?

Survival Rate, %

unadjusted

adjusted

year

Japan

Europe

USA

Japan

Europe

USA

unadjusted

adjusted

year

Survival Rate, %

Japan

Europe

USA

KDIGO

Am J Kidney Dis 44:S16-S21, 2004
ANNUAL CRUDE DEATH RATE IN JSDT
AGE-ADJUSTED DEATH RISK (REF. 2008) BY M. WAKASUGI

Male

Female
# Unique to Japan: Practice Pattern (DOPPS)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Unique to Japan: practice pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular Access</td>
<td>Almost all AVF</td>
</tr>
<tr>
<td>Anemia</td>
<td>Lower Hb, EPO dose, Fe prescription</td>
</tr>
<tr>
<td>CKD MBD</td>
<td>Low vitamin D injection (vs. USA)</td>
</tr>
<tr>
<td>HD Regimen</td>
<td>Lower Blood flow rate, low Kt/V</td>
</tr>
<tr>
<td>Dialysate</td>
<td>High Na, low bicarbonate</td>
</tr>
<tr>
<td>CVD</td>
<td>Relatively higher BP</td>
</tr>
<tr>
<td>Labs.</td>
<td>Frequents checks; CRP, Chest X-ray, vascular calcification</td>
</tr>
</tbody>
</table>

CKD-MBD GUIDELINES AND NEW DRUGS

- 2014 May 12: Ferric Citrate Hydrate, po
- 2016 Dec 19: Etelcalcetide Hydrochloride, iv
- 2017 KDIGO CKD-MBD CPG. Kidney Int 7;1-59, 2017
JAPANESE SOCIETY FOR DIALYSIS THERAPY (JSDT) : CPG FOR CKD-MBD

- Guideline working group, Japanese Society for Dialysis Therapy: Clinical practice guideline for the management of secondary hyperparathyroidism in chronic dialysis patients.
  Ther Apher Dial 12: 511-522, 2008
- Clinical practice guideline for the management of chronic kidney disease-mineral and bone disorder.
  Ther Apher Dial 17:247-288, 2013

“JSHT recommended very different PTH target from the KDIGO and emphasized the parathyroid interventions in their recommendation.”

Tsukamoto Y. Clin Calcium 24(12):1757-1761, 2014
EVIDENCE-BASED DIALYSIS?

Pro: The value of RCT in dialysis methods (Ajay K Singh & Jameela A Kari)
Con: RCT have failed in the study of dialysis methods
(Zbylut J Twardowski & Madhukar Misra)

Polar Views in Nephrology: Moderator’s view:
Are alternative dialysis strategies superior to conventional dialysis:
what Popper tells us...(Wim Van Biesen & Norbert Lameire)

NO RCT in Dialysis Therapy!
Experience-Based (Conventional HD)

NUMBER OF RANDOMIZED CONTROLLED TRIALS

Archdeacon et al. CJASN 2013
SHIFT OUR RESEARCH FOCUS

1. More qualitative methods used in social sciences
2. More patient-reported outcomes
3. Unmet needs for studies to elucidate racial and ethnic differences in QOL issues
4. Research and policy changes should be driven by experienced practitioners with current patient contact to ensure that they are relevant to patient needs
5. Support research to improve QOL and discourage cookie-cutter survival studies
6. QOL metrics (pain, depression,..) needs to be incentivized in clinical practice to drive related research efforts.

Lee MB and Bargman JM. CJASN 11:1083-7, 2016
MULTIDIMENSIONAL MEASURE OF DIALYSIS. HR, HEART RATE.

Multidimensional Assessment Of Optimal Dialysis: Potential Measures

- Patient reported Outcomes
- Small solute removal
- Residual Kidney Function
- Left Ventricular Geometry
- Ultrafiltration Rate and Extracellular Fluid Volume Management
- Higher weight range middle molecule removal
- Phosphorus
- HR and BP Variability
- Serum Potassium Control

Potential Dialytic Strategies To Achieve

- Treatment Duration
- Treatment Frequency
- Incremental Dialysis
- Preservation of Residual Kidney Function
- Consideration of Home Dialysis

Goals of ESRD Care

- Maximize Quality of Life
- Maximize Survival

PATIENT REPORTED OUTCOME (PRO)

- Medicine: Efficacy, Safety, Outcome
- Outcome:
  - Hard: Death, CVD, ESRD
  - Effectiveness (PRO)
- QOL (HROOL): SF-36, EQ-5D

Drug A: Pulmonary hypertension
6 min walk distance: +31 meter (Effective!!)
Cost: >250 dollars per day
Randomized trials provide the most reliable evidence about the safety and effectiveness of interventions to improve health care and patient outcomes. Unfortunately, the potential for trials to inform treatment decisions remains limited because the outcomes reported often do not resonate with what is directly meaningful and relevant to patients and their clinicians [1–3].

Further, inconsistent reporting of outcomes across trials prevents assessment of the comparative effect of interventions [4]. Outcome reporting bias, whereby authors cherry-pick the outcomes they report on the basis of favorable results, may also occur when there is not a standardized list of outcomes measured and reported [5, 6]. Collectively these problems may undermine the reliability of published trials, leading to inefficient use of scarce research and health care resources and unintended harm to...
UNIQUENESS OF ASIAN PEOPLE RELATED TO CKD-MBD

Diet & Dietary habit (protein, calorie,)
Life-style (exercise, sleep,)
Socio-economic status
  (family, income, education,)
Genetics (ethnic difference,)
Others (drugs, public support,)

More International Cohorts studies like DOPPS, ARC, and National registries are required.