Target blood pressure for Asian population: New Answers from the Recent Study Results

Park Sungha
Yonsei University Health System
Cardiovascular Hospital
Division of Cardiology
SPRINT primary outcome

Hazard ratio with intensive treatment, 0.75 (95% CI, 0.64–0.89)

Cumulative Hazard

No. at Risk
Standard treatment 4683 4437 4228 2829 721
Intensive treatment 4678 4436 4256 2900 779

Years
What is the treatment target in the general hypertension population in Asia?
Is a systolic blood pressure target <140 mmHg indicated in all hypertensives? Subgroup analyses of findings from the randomized FEVER trial

Zhang Y et al. Eur Heart J 2011;32:1500-1508

4850 out of 9711 hypertensives (SBP 138 vs 142)

![Graph showing the proportion of patients with events over time](image)
Korean National Health Insurance Cohort Registry (N=40917, no CVD, DM or CKD)
Prevention of cardiovascular events with calcium channel blocker-based combination therapies in patients with hypertension: a randomized controlled trial

Matsuzaki M et al. J Hypertens 2011;29:1649-1659

3501 hypertensives FU for 3.61 years

Hazard ratio Log-Rank test
Contrast Estimate (95%C.I.) P value
BB/ARB 1.66 (0.90 3.04) 0.0770
ARB/TD 1.39 (0.67 2.92) 0.4453
BB/TD 2.31 (1.17 4.56) 0.0109

Number at risk
Benidipine plus BB 1089 1065 1023 998 974 947 921 612 310
Benidipine plus ARB 1110 1097 1069 1049 1030 1008 987 649 329
Benidipine plus TD 1094 1071 1044 1027 1011 998 966 630 327
HT treatment in hypertensives not at high cardiovascular risk

- Anti hypertensive treatment should be considered in hypertensive subjects with mild to moderate risk

- Target blood pressure should be < 140/90mmHg

- Any of the five first class agents may be used but combination of CCB + BB may be inferior in terms of stroke reduction
Treatment target in diabetes and CKD
Primary Outcome
Nonfatal MI, Nonfatal Stroke or CVD
Death

HR = 0.88
95% CI (0.73–1.06)

ACCORD Double 2 x 2 Factorial Design
Nonfatal Stroke

HR = 0.63
95% CI (0.41–0.96)

Total Stroke

HR = 0.59
95% CI (0.39–0.89)

Difference in the relationship between blood pressure and CV events according to race.
Relation between CV complications and BP level: Challenge-DM study

16,869 patients in nationwide registry: 29 months FU

Kawamori R et al. DRCP 2009;83:241-248
Intensive Blood-Pressure Control in Hypertensive Chronic Kidney Disease

Interaction of CKD and HT for development of CVD (SUITA study)

5494 individuals (ages 30 to 79, No MI or stroke)
Primary Outcome Experience in the Six Pre-specified Subgroups of Interest

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>HR</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0.75 (0.64, 0.89)</td>
<td></td>
</tr>
<tr>
<td>No Prior CKD</td>
<td>0.70 (0.56, 0.87)</td>
<td>0.36</td>
</tr>
<tr>
<td>Prior CKD</td>
<td>0.82 (0.63, 1.07)</td>
<td></td>
</tr>
<tr>
<td>Age &lt; 75</td>
<td>0.80 (0.64, 1.00)</td>
<td>0.32</td>
</tr>
<tr>
<td>Age ≥ 75</td>
<td>0.67 (0.51, 0.86)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.84 (0.62, 1.14)</td>
<td>0.45</td>
</tr>
<tr>
<td>Male</td>
<td>0.72 (0.59, 0.88)</td>
<td></td>
</tr>
<tr>
<td>African–American</td>
<td>0.77 (0.55, 1.06)</td>
<td>0.83</td>
</tr>
<tr>
<td>Non African–American</td>
<td>0.74 (0.61, 0.90)</td>
<td></td>
</tr>
<tr>
<td>No Prior CVD</td>
<td>0.71 (0.57, 0.88)</td>
<td>0.39</td>
</tr>
<tr>
<td>Prior CVD</td>
<td>0.83 (0.62, 1.09)</td>
<td></td>
</tr>
<tr>
<td>SBP ≤ 132</td>
<td>0.70 (0.51, 0.95)</td>
<td>0.77</td>
</tr>
<tr>
<td>132 &lt; SBP &lt; 145</td>
<td>0.77 (0.57, 1.03)</td>
<td></td>
</tr>
<tr>
<td>SBP ≥ 145</td>
<td>0.83 (0.63, 1.09)</td>
<td></td>
</tr>
</tbody>
</table>

*Treatment by subgroup interaction
*Unadjusted for multiplicity

### Renal outcome in the SPRINT trial

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive treatment</th>
<th>Standard treatment</th>
<th>HR(95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients(%)</td>
<td>% per year</td>
<td>Patients(%)</td>
<td>% per year</td>
</tr>
<tr>
<td><strong>CKD</strong> <em>(N = 1330)</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite renal outcome</td>
<td>14(1.1)</td>
<td>0.33</td>
<td>15(1.1)</td>
<td>0.36</td>
</tr>
<tr>
<td>≥ 50% reduction of eGFR</td>
<td>10(0.8)</td>
<td>0.23</td>
<td>11(0.8)</td>
<td>0.26</td>
</tr>
<tr>
<td>Dialysis</td>
<td>6(0.5)</td>
<td>0.14</td>
<td>10(0.8)</td>
<td>0.24</td>
</tr>
<tr>
<td>KT</td>
<td>0</td>
<td></td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Incident albuminuria</td>
<td>49/526(9.3)</td>
<td>3.02</td>
<td>59/500(11.8)</td>
<td>3.90</td>
</tr>
<tr>
<td><strong>W/O CKD</strong> <em>(N=3332)</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 30% reduction in eGFR to &lt; 60ml/min</td>
<td>127(3.8)</td>
<td>1.21</td>
<td>37(1.1)</td>
<td>0.35</td>
</tr>
<tr>
<td>Incident albuminuria</td>
<td>110/1769(6.2)</td>
<td>2.00</td>
<td>135/1831(7.4)</td>
<td>2.41</td>
</tr>
</tbody>
</table>
Target BP in DM and CKD

For diabetes a target SBP of 140mmHg is recommended → However, SBP below 130mmHg can be considered in high risk diabetes if tolerated

For patients with CKD: target BP of < 130/80 should be considered
BP target in the elderly
Japanese Trial to Assess Optimal Systolic Blood pressure in Elderly Hypertensive Patients (JATOS)

- Patients with essential hypertension (65-85 years of age with SBP > 160mmHg)

- 2212 patients with strict treatment of SBP < 140mmHg and usual treatment (140-159mmHg)

- Primary endpoint of cardiovascular disease and renal failure

Hypertens Res 2008;31(12):2115-2127

Hypertens Res 2008;31:2115-2127
Japanese Trial to Assess Optimal Systolic Blood pressure in Elderly Hypertensive Patients (JATOS)

Hypertens Res 2008;31(12):2115-2127

Hypertens Res 2008;31:2115-2127
Subgroup analyses of the elderly in the FEVER trial

6532 out of 9711 hypertensives (SBP 138 vs 142)

HR = 0.56, 95% CI 0.41-0.75, p = 0.0001

Zhang Y et al. Eur Heart J 2011;32:1500-1508
Target BP in the elderly

- All hypertension in non-frail elderly should be treated with anti hypertensive medications.

- There should be an initial target SBP of < 150mmHg.

- Patients who tolerate additional lowering may have their SBP lowered to below 130-140mmHg.
BP target in HT with CAD and HT at high risk of CAD
J curve in HT patients with CAD

22,576 patients with HT and CAD

Low DBP may not be an independent risk for cardiovascular death in revascularized coronary artery disease patients

Hisashi Kai\textsuperscript{a}, Takafumi Ueno\textsuperscript{b}, Takeshi Kimura\textsuperscript{c}, Hisashi Adachi\textsuperscript{d}, Yutaka Furukawa\textsuperscript{e}, Toru Kita\textsuperscript{e}, Tsutomu Imaizumi\textsuperscript{a}, on behalf of CREDO-Kyoto Investigators

\textbf{Kai H et al. J Hypertens 2011;29:1889-1896}

7180 stable CAD (Median FU: 3.6 years) Adjusted for age, sex, eGFR, heart failure, prior CVD, PP, LV systolic dysfunction, prior MI

\begin{figure}
\centering
\includegraphics[width=\textwidth]{chart.png}
\caption{Cardiovascular death}
\end{figure}
Relationship between the achieved blood pressure and the incidence of cardiovascular events in Japanese hypertensive patients with complications: a sub-analysis of the CASE-J trial


Patients with DM, CKD or LVH (85% of 4553 subjects)

**P<0.01, ***P<0.001, SBP: vs. <130 mm Hg; DBP: vs. 75–79 mm Hg**
Target BP in previous CVD and/or patients at high risk of CVD

- Consideration for target BP < 130/80 mmHg should be given

- All first line agents may be used unless there are compelling indication to use certain class of medications
Blood-pressure targets in patients with recent lacunar stroke: the SPS3 randomised trial

The SPS3 Study Group*

3020 subjects with recent lacunar infarct

Open label: SBP < 130(127mmHg) vs SBP; 130-149(138mmHg)

Non significant reduction in stroke (HR: 0.81, 95% CI: 0.64-1.03, P = 0.08)

Composite outcome of stroke, MI or vascular death (HR: 0.84, 0.68-1.04, P = 0.32)

Significant reduction of ICH (HR: 0.37, 0.15-0.95, P = 0.03)
Effects of Blood Pressure Lowering on Intracranial and Extracranial Bleeding in Patients on Antithrombotic Therapy

The PROGRESS Trial

Arima H et al. Stroke 2012;43:1675–1677

N = 6105, FU; 3.9 years
Blood Pressure Levels and Bleeding Events During Antithrombotic Therapy
The Bleeding With Antithrombotic Therapy (BAT) Study

Toyoda K et al. Stroke 2010;41:1440-1444
N=4001, Median FU: 19 months
Optimal cutoff level for increased risk of ICH ≥ 130/81mmHg
How much should recent clinical trials, including SPRINT, impact the target BP in Asia?
No changes in target BP for

- Previous stroke
- Hypertensive subjects under the age of 50
- Low risk hypertensives without history of CHD or CKD with Framingham risk score less than 15
- What about diabetes?, CKD with proteinuria?
SBP target can be lowered to below 130mmHg if tolerated for:

- Patients over the age of 50 with previous CHD
- High risk hypertensives over the age of 50 without previous history of CHD or MI
- Non frail elderly hypertensives
- Chronic kidney disease
- Patients undergoing antplatelet, antithrombotic therapy
- High risk diabetics in the asian population?
Thank you very much for your attention
Meta regression analysis of 21 studies with > 480,000 patient years

Thiazide like diuretics associated with 12% additional reduction of CV events ($P=0.049$) and 21% additional reduction of heart failure ($P=0.023$)

Thiazide type diuretics did not reduce coronary events or all cause mortality
2009 ESH guidelines

*Abbreviations of trials: M.HOPE; MICROHOPE; ABCD (HT, hypertensives; NT, normotensives); IDNT, IDNT (IR, irbesartan; AM, amlodipine); REN, RENAAL; PROG, PROGRESS; ADV, ADVANCE; ACC, ACCESS; PROF, PROFESS; PREV, PREVENT; EU, EUROPA; ACT, ACTION; CAM, CAMELOT

Important differences compared with previous guidelines: DM

Lowering BP < 130/80mmHg in high-risk patients (diabetes or a history of CV or renal disease) is not supported by RCT evidence.

In diabetes, HOT, UKPDS trials showing benefits from DBP reductions to between 80–85mmHg
- No trial where SBP was reduced < 130mmHg
- ‘normotensive’ABCD study is very small and showed benefit only in secondary endpoint

Target BP in diabetes: 140/85(ESC, KSH)

What about JNC VIII?: 140/90

ESC/ESH guideline 2013
Systolic Pressures (mean ± 95% CI)

Average after 1st year: 133.5 Standard vs. 119.3 Intensive, Delta = 14.2

Mean # Meds
Intensive: 3.2 3.4 3.5 3.4
Standard: 1.9 2.1 2.2 2.3

Int. N = 2174
Std. N = 2208

### Kidney Disease: Improving Global Outcomes (KDIGO) 2012 guideline for HT management in CKD

<table>
<thead>
<tr>
<th>Albuminuria</th>
<th>BP target</th>
<th>Preferred agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30 mg/day</td>
<td>≤ 140/90mmHg</td>
<td>None</td>
</tr>
<tr>
<td>30-300 mg/day</td>
<td>≤ 130/80mmHg</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td>&gt; 300 mg/day</td>
<td>≤ 130/80mmHg</td>
<td>ACEI or ARB</td>
</tr>
</tbody>
</table>

Kidney Int 2012;2(Suppl):337-414
Target Blood Pressure for Treatment of Isolated Systolic Hypertension in the Elderly

Valsartan in Elderly Isolated Systolic Hypertension Study

Ogihara T et al. Hypertension 2010;56:196-202

A

- Moderate control group (12.0/1000 patients-year)
- Strict control group (10.6/1000 patients-year)

p = 0.383 (log-rank test)
Hazard ratio (95% CI): 0.89 (0.60-1.31)
Blood pressure target in subjects with previous CVD

**ACCORD Double 2 x 2 Factorial Design**

<table>
<thead>
<tr>
<th></th>
<th>Lipid</th>
<th>BP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Placebo</strong></td>
<td>1383</td>
<td>1178</td>
</tr>
<tr>
<td><strong>Fibrate</strong></td>
<td>1374</td>
<td>1193</td>
</tr>
<tr>
<td><strong>Intensive Glycemic Control</strong></td>
<td>1370</td>
<td>1184</td>
</tr>
<tr>
<td></td>
<td>1391</td>
<td>1178</td>
</tr>
<tr>
<td><strong>Standard Glycemic Control</strong></td>
<td>2753</td>
<td>2362</td>
</tr>
<tr>
<td></td>
<td>2765</td>
<td>2371</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>5518</td>
<td>4733*</td>
</tr>
</tbody>
</table>

* 94% power for 20% reduction in event rate, assuming standard group rate of 4% / yr and 5.6 yrs follow-up

**ACCORD study group. N Engl J Med 2010**
Reduction in Microalbuminuria as an Integrated Indicator for Renal and Cardiovascular Risk Reduction in Patients With Type 2 Diabetes

Shin-ichi Araki,¹ Masakazu Haneda,² Daisuke Koya,³ Hideki Hidaka,⁴ Toshiro Sugimoto,¹ Motohide Isono,¹ Keiji Isshiki,¹ Masami Chin-Kanasaki,¹ Takashi Uzu,¹ and Atsunori Kashiwagi¹