Hypertension club
review of literature

By
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Usefulness of HR to Predict Cardiac Events in Treated Patients With High-Risk Systemic Hypertension
Stevo Julius, et al, Am J Cardiol 2012

• In VALUE trial 4 key issues explored:
  • First, HR associated with adverse outcomes.
  • Second, Increased risk remained significant after adjustment for (BP) levels and other risk factors.
  • Third, Whether risk would persist across 5-years.
  • Fourth: Effective BP control decreases CV risk attributable to tachycardia.
15,193 high risk HTN enrolled in the (VALUE) trial, FU for 5 y.

- Primary end point for a 10-beats/min of the baseline HR increment was 1.16 (95% confidence interval 1.12 to 1.20).

- (Stevo Julius, et al, 2012)
Primary endpoint

% of patients with an event

1st year: 15193, 381
2nd year: 14477, 320
3rd year: 13826, 354
4th year: 13083, 333
5th year: 11845, 200

Heart failure

1st year: 15193, 176
2nd year: 14853, 146
3rd year: 14009, 166
4th year: 13343, 169
5th year: 12146, 92

All cause deaths

1st year: 15193, 253
2nd year: 14727, 297
3rd year: 14252, 374
4th year: 13683, 411
5th year: 12555, 277

* = Highest quintile (5)
** = Average quintiles 1-4

Total population

= Total endpoints
Ivabradine in (BEAUTIFUL) reduced reinfarction.

In Systolic CHF (SHIFT), decreased CV death.

The effect was significant only in patients with a faster HR.

Thus, pacemaker deceleration might also be useful in tachycardia and high-risk hypertension has not yet been tested in a prospective randomized trial.

Stevo Julius, et al. 2012)
Conclusion

- Increased HR is a long-term predictor of CV events in high-risk HTN, not modified by good BP control.

- It is not yet known whether a therapeutic reduction of HR would improve CV prognosis.

(Stevo Julius, et al, 2012)
Diagnosed HTN in Canada:

Incidence, prevalence and associated mortality:

Cynthia Robitaille MSc, et al, CMAJ 2012.
Figure 1: Prevalence and incidence of diagnosed hypertension among adults aged 20 years and older from 1998/99 to 2007/08 in Canada. The rates have been age-standardized to the 1991 Canadian population.
Figure 5: All-cause annual mortality and rate ratios in 2007/08 among adults aged 20 years and older with and without diagnosed hypertension, by age. Error bars indicate 95% confidence intervals.
Conclusion

- The number of people living with diagnosed hypertension has increased steadily from 1998/99 to 2007/8, incidence slightly declined.
- Programs to improve the lifestyles of Canadians, such as the proposed initiative to reduce sodium consumption, will be critical to decrease HTN.
- This study highlights the need to continue tracking diagnosed hypertension to provide timely surveillance information that can be used to enhance prevention and management programs.
The 2012 CHEP Recommendations

What’s new in the treatment of hypertension?

What’s still really important?
CHEP 2012 Recommendations

What’s new?

• 1) Out-of-office BP measurements are important in both diagnosis and management.

• 2) With nondiabetic CKD, target BP < 140/90

• 3) For patients with systolic dysfunction and hypertension: ACE-i, BB and (for most) aldosterone antagonists are recommended.
The 2012 CHEP Recommendations

What’s still important?

1) Lifestyle changes are a critical component of hypertension management and prevention

2) The most important step in prescription of antihypertensive therapy is achieving patient “buy-in”

3) Single pill combinations help achieve blood pressure control

4) The management of HTN is all about global CV risk management and vascular protection
## Impact of lifestyle therapies on BP

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Targeted change</th>
<th>Expected BP change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium reduction</td>
<td>&lt; 1500 mg/day</td>
<td>-5 / -3</td>
</tr>
<tr>
<td>Weight loss</td>
<td>BMI &lt; 25 kg/m²</td>
<td>-7 / -6</td>
</tr>
<tr>
<td>Alcohol reduction</td>
<td>&lt; 2 drinks/day</td>
<td>-5 / -2</td>
</tr>
<tr>
<td>Exercise</td>
<td>4+ times/week</td>
<td>-5 / -4</td>
</tr>
<tr>
<td>Dietary patterns</td>
<td>DASH diet</td>
<td>-11 / -6</td>
</tr>
</tbody>
</table>

Result of aggregate and metaanalyses of short term trials.

Meta analysis on different reductions in dietary sodium intake on BP


![BP reduction vs mg/day reduction in sodium](image-url)
High sodium intake increases risk of hypertension-related complications

STITCH Study: cluster randomization

27 practices

2048 patients

18 practices

Recommendations-Based Care

Algorithm-Based Care featuring early use of SPCs

Feldman et al, Hypertension 2009
STITCH: Primary Outcome
Proportion of Practice at BP Target

$p = 0.03$

Absolute Difference in BP control rate = 12%
CHEP recommendations regarding drug combinations

**Adherence:** improved by single pill combinations

**CHD:** ACE-I and a dihydropyridine CCB is preferable to an ACE-I and a diuretic.

**With Diabetes:** ACE-I (ARB) considered, a dihydropyridine CCB is preferable to a thiazide.
Adherence to antihypertensive management can be improved by a multi-pronged approach

- Assess adherence to pharmacological and non-pharmacological therapy at every visit
- Teach patients to take their pills on a regular schedule associated with a routine daily activity e.g. brushing teeth.
- Replacing multiple pill antihypertensive combinations with single pill combinations
Adherence to antihypertensive management can be improved by a multi-pronged approach:

- Encourage regular monitoring of BP.
- Educate patients and patients' families about their disease/treatment regimens verbally and in writing.
- Use an interdisciplinary care approach coordinating with worksite health care givers and pharmacists if available.
Assess global cardiovascular risk in all hypertensive patients

91% of hypertensive patients have at least 1 additional risk factor

↑ Risk factors = ↑ Global CV risk

2012 CHEP Recommendations
Assessing CV risk to improve adherence

Informing patients of their global risk to improve the effectiveness of risk factor modification.

Using analogies that describe comparative risk such as “Cardiovascular Age”, “Vascular Age” or “Heart Age” to inform patients of their risk status.
What is vascular age?

• The age of the vascular system of a patient, based on the aggregate of their cardiovascular risk factors.

• This age is calculated as the age a person would be with the same calculated cardiovascular risk but whose risk factors were all within normal ranges.
Impact of discussing coronary risk with patients on blood pressure treatment

<table>
<thead>
<tr>
<th>Blood pressure drop (mmHg)</th>
<th>Receiving more intensive treatment (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Usual treatment</strong></td>
<td><strong>Risk counselling</strong></td>
</tr>
<tr>
<td>5</td>
<td>13</td>
</tr>
<tr>
<td>10</td>
<td>27</td>
</tr>
<tr>
<td>15</td>
<td>34</td>
</tr>
</tbody>
</table>

Only relying on manual office blood pressures misses out on white coat and masked hypertension

From Pickering, Hypertension 1992
The prognosis of masked hypertension

Prevalence is approximately 10% in HTN patients.

Bobrie et al. JAMA 2004;291:1342-9
Criteria for the diagnosis of hypertension and recommendations for follow-up

- **Clinic BP**
  - Hypertension visit 3
    - \( \geq 160 \text{ SBP or } \geq 100 \text{ DBP} \):
      - Diagnosis of HTN
    - \(< 160 / 100\):
      - ABPM or HBPM
  - Hypertension visit 4-5
    - \(\geq 140 \text{ SBP or } \geq 90 \text{ DBP} \):
      - Diagnosis of HTN
    - \(< 140 / 90\):
      - Continue to follow-up

- **ABPM (If available)**
  - Awake BP
    - \(< 135/85\):
      - Continue to follow-up
    - \(\geq 135 \text{ SBP or } \geq 85 \text{ DBP} \):
      - Diagnosis of HTN

- **Home BPM**
  - \(< 135/85\):
    - Continue to follow-up
  - \(\geq 135/85\):
    - Diagnosis of HTN
    - Confirm with repeat Home BPM or ABPM

Patients with high normal blood pressure (clinic SBP 130-139 and/or DBP 85-89) should be followed annually.
## Confirming the diagnosis of white coat hypertension

<table>
<thead>
<tr>
<th>CHEP 2011</th>
<th>CHEP 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Using home BP measurements (see recommendation Home Measurement of BP), patients can be diagnosed as hypertensive if the average SBP is $\geq 135$ mmHg or the DBP is $\geq 85$ mmHg (Grade C). If the average home BP is less than 135/85 mmHg, it is advisable to perform 24h ABPM to confirm that the mean 24h ABPM is $&lt;130/80$ mmHg and the mean awake ABPM is $&lt;135/85$ mmHg before diagnosing white coat hypertension (Grade D).</td>
<td>Using home BP measurements, hypertensive: BP $&gt;135/85$ mmHg. If $&lt;135/85$ mmHg, repeat or ABPM to confirm that the mean 24h ABPM is $&lt;130/80$ mmHg and the mean awake ABPM is $&lt;135/85$ mmHg before diagnosing white coat hypertension.</td>
</tr>
</tbody>
</table>
In 2012, CHEP revisited the CKD BP targets following publication of significant new data.

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>For patients with nondiabetic chronic kidney disease, target BP is &lt;130/80 mm Hg (Grade C).</td>
<td>For patients with nondiabetic CKD, target BP is &lt;140/90 mm Hg (Grade B).</td>
</tr>
</tbody>
</table>
PRIMARY OUTCOME: rate of change in GFR (slope)
AASK Summary

- No benefit of targeting a BP of 125/75 mmHg compared to 140/90 mmHg with respect to rate of decline in kidney function in African Americans

No difference in risk of secondary endpoints
- Kidney failure
- Death
- Kidney failure or death
- 50% decline in GFR, kidney failure, or death
AASK re-analysis suggests that patients with proteinuria did better with lower BP (based on a secondary endpoint).

Appel LJ et al. NEJM 2010
### Results of efficacy outcomes in RCT’s of blood pressure targets in adults with CKD

<table>
<thead>
<tr>
<th>Outcome</th>
<th>MDRD Study</th>
<th>AASK Trial</th>
<th>REIN-2 Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥50% (or ≥25 mL/min per 1.73 m²) decrease in GFR, kidney failure, or death*</td>
<td>-</td>
<td>Risk reduction, 2% (95% CI, -22% to 21%); $P = 0.85$; HR, 0.91 (CI, 0.77 to 1.08); $P = 0.27$</td>
<td>-</td>
</tr>
<tr>
<td>Kidney failure or death</td>
<td>Study A: RR, ND; $P &gt; 0.05$; HR, 0.77† (CI, 0.65 to 0.91); $P = 0.33$</td>
<td>Risk reduction, 12% (CI, -13% to 32%); $P = 0.31$; HR, 0.85 (CI, 0.71 to 1.02); $P = 0.08$</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Study B: RR, 0.85 (CI, 0.60 to 1.22); $P = 0.33$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50% decrease in GFR or kidney failure‡</td>
<td>-</td>
<td>Risk reduction, -2% (CI, -31% to 20%); $P = 0.87$; HR, 0.95 (CI, 0.78 to 1.15); $P = 0.59$</td>
<td>-</td>
</tr>
<tr>
<td>Kidney failure</td>
<td>HR, 0.76 (CI, 0.52 to 1.10); $P = 0.15$</td>
<td>Risk reduction, 6% (CI, -29% to 31%); $P = 0.72$</td>
<td>23% vs. 20%; $P = 0.99$</td>
</tr>
<tr>
<td></td>
<td>HR, 0.68† (CI, 0.57 to 0.82); $P &lt; 0.001$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality, %</td>
<td>2 vs. 1; $P = ND$</td>
<td>2 vs. 2; $P = ND$</td>
<td>2 vs. 1; $P = ND$</td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>-</td>
<td>HR, 0.98 (CI, 0.48 to 2.01); $P = 0.96$</td>
<td>1% vs. 1%; $P = ND$</td>
</tr>
<tr>
<td>CVD events</td>
<td>RR, 1.03§ (CI, 0.59 to 1.79)</td>
<td>2% vs. 3%; $P = ND$</td>
<td>-</td>
</tr>
<tr>
<td>Rate of annual GFR decline, mL/min per 1.73 m²</td>
<td>Study A: 1.61 (CI, -0.8 to 3.9); $P = 0.18$</td>
<td>0.26∥ (CI, -0.21 to 0.64); $P = 0.25$</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Study B: 0.5∥ (CI, -0.4 to 1.4); $P = 0.28$</td>
<td></td>
<td>-</td>
</tr>
</tbody>
</table>

**Aldosterone antagonists in CHF**

<table>
<thead>
<tr>
<th>CHEP 2011</th>
<th>CHEP 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. In patients with systolic dysfunction, ACE inhibitors (Grade A) and betablockers (Grade A) are recommended for initial therapy. Aldosterone antagonists (Grade B) are also recommended for patients with NYHA Class III or IV symptoms of heart failure or post myocardial infarction.</td>
<td><strong>EF &lt;40%, ACE-I (Grade A) and BB. (Grade A) are recommended for initial therapy; Aldosterone antagonists may be added for patients with a recent CV hospitalization, AMI, elevated BNP or NT-proBNP level, or NYHA class II to IV symptoms (Grade A). Careful monitoring for hyperkalemia.</strong></td>
</tr>
</tbody>
</table>

*EF* = Ejection Fraction; *ACE-I* = Angiotensin-Converting Enzyme Inhibitors; *BB. = Beta-blockers; *CHF* = Congestive Heart Failure; *AMI* = Acute Myocardial Infarction; *BNP* = Brain Natriuretic Peptide; *NT-proBNP* = N-Terminal Pro-BNP; *NYHA* = New York Heart Association
Aldosterone antagonists reduce mortality rates in systolic heart failure

**RALES**

- Spironolactone
- Placebo

**EMPHASIS-HF**

- Placebo
- Eplerenone

**EPHESUS**

- Placebo
- Eplerenone

Pitt B, NEJM 1999;
Pitt B NEJM 2003;
Zannad F NEJM 2010
Meta-analyses examining SBP targets < 140mmHg in patients with diabetes

Bangalore et al. Circ 2011
- Included only trials that achieved SBPs < 140 mmHg
- Outcomes were mortality, CV mortality, MI, HF and stroke

Reboldi et al. J Hypertens 2011
- Included all anti-hypertensive trials
- Outcomes were MI and stroke only
### Results

Mortality increased at SBP <130 and >135, Stroke continued to decrease beyond 130

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Achieved blood pressure ≤ 135 mmHg</th>
<th>Achieved blood pressure ≤ 130 mmHg</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># studies</td>
<td>OR (95% CI)</td>
<td># studies</td>
</tr>
<tr>
<td>Mortality</td>
<td>6</td>
<td>0.87 (0.79-0.95)</td>
<td>6</td>
</tr>
<tr>
<td>CV Mortality</td>
<td>4</td>
<td>0.9 (0.78-1.03)</td>
<td>3</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>4</td>
<td>0.92 (0.76-1.11)</td>
<td>4</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>3</td>
<td>0.82 (0.66-1.02)</td>
<td>3</td>
</tr>
<tr>
<td>Stroke</td>
<td>5</td>
<td>0.90 (0.78-1.03)</td>
<td>4</td>
</tr>
</tbody>
</table>

Bangalore et al, Circulation 2011; 123:2799-2810
What’s new?

- **Out-of-office** blood pressure measurements are important in both the diagnosis and management of hypertension.

- For patients with nondiabetic chronic kidney disease, target blood pressure should be \(< 140/90\) mmHg.

- For patients with systolic dysfunction and hypertension, ACE inhibitors, beta-blockers and (for most) aldosterone antagonists are recommended.
What’s still important?

- **Lifestyle changes** are a critical component of hypertension management and prevention.
- The most important step in prescription of antihypertensive therapy is achieving patient “buy-in”.
- **Single pill** combinations help achieve blood pressure control.
- The management of hypertension is all about global cardiovascular risk management and vascular protection.
• For your patients – ask them to sign up at www.myBPsite.ca for free access to the latest information & resources on high blood pressure

• For health care professionals – sign up at www.hypertension.ca for automatic updates and information on current hypertension educational resources