Overview of Undiagnosed/ Masked Hypertension

Jackson T. Wright Jr., MD, PhD
Emeritus Professor
Case Western Reserve University School of Medicine
Co-Lead Team Best Practices, Cardi-OH

The Ohio Cardiovascular Health Collaborative is funded by the Ohio Department of Medicaid and administered by the Ohio Colleges of Medicine Government Resource Center. The views expressed in this presentation are solely those of the authors and do not represent the views of the state of Ohio or federal Medicaid programs.
Objectives

• Provide an overview of the prevalence and impact of Masked Hypertension (MH) on cardiovascular outcomes
• Summarize the risk factors and diagnostic evaluation for MH
• Recognize treatment implications in patients with MH
Significance of Out of Office Blood Pressure (BP) Readings

• The primary reason is to identify patients not on antihypertensive medication with:
  • White Coat Hypertension (WCH) with elevated office BPs who may not require drug treatment.
  • Masked Hypertension (MH) with normal office readings who should be considered for drug treatment.

• In addition, for patients on antihypertensive medications, to identify:
  • White Coat Effect (WCE) – where office BPs are significantly higher than out of office readings.
  • Masked Uncontrolled Hypertension (MUCH) – where office readings indicate adequate BP control but out of office readings are elevated.
White Coat Hypertension (WCH) and Masked Hypertension (MH)

• The prevalence of WCH and MH is between 10-30% each depending on the study.

• The risk of cardiovascular morbidity and mortality for MH is about the same as adults with sustained hypertension, indicating a benefit to treatment.

• While there appears to be an increased risk of cardiovascular morbidity with MH, we do not know if there is a benefit to treating these individuals.

*Up to 30% of patients in our practices are either over or under-treated for hypertension.*

http://www.onlinejacc.org/content/accj/71/19/2199.full.pdf
Characteristics of Masked Hypertension

- MH prevalence averages ~ 13% and up to 30% in some surveys.
- Prevalence increases with higher (normal) office readings.
- Increased prevalence of MH is also seen in older persons, males, Blacks, and those with obesity, diabetes, chronic kidney disease (CKD), and sleep apnea.
- Large longitudinal cohort studies show CVD risk is similar to that of sustained hypertension.
- Overlap between MH identified by home blood pressure monitoring (HBPM) and ambulatory blood pressure monitoring (ABPM) is only 60-75% though both show same cardiovascular disease (CVD) risk compared to never-treated hypertensives (NTH) and sustained hypertension (HTN).
- Randomized controlled trial (RCT) data evaluating benefit of treatment is not yet available.
- Profiles of risk for treated patients showing MUCH parallel that of MH, respectively.
CVD and Mortality with Masked HTN vs. Normotension

A

Composite cardiovascular events: masked HTN versus normotension

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Masked hypertension</th>
<th>Normotension</th>
<th>Odds ratio M-H, fixed, 95% CI</th>
<th>Odds ratio M-H, fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Asayama et al22</td>
<td>149</td>
<td>1612</td>
<td>159</td>
<td>4176</td>
</tr>
<tr>
<td>Bjorklund et al27</td>
<td>10</td>
<td>82</td>
<td>10</td>
<td>188</td>
</tr>
<tr>
<td>Booth et al26</td>
<td>35</td>
<td>352</td>
<td>10</td>
<td>329</td>
</tr>
<tr>
<td>Fagard et al25</td>
<td>7</td>
<td>31</td>
<td>20</td>
<td>136</td>
</tr>
<tr>
<td>Hansen et al30</td>
<td>21</td>
<td>211</td>
<td>48</td>
<td>859</td>
</tr>
<tr>
<td>Mancia et al29</td>
<td>25</td>
<td>184</td>
<td>43</td>
<td>909</td>
</tr>
<tr>
<td>Pierdomenico et al11</td>
<td>11</td>
<td>120</td>
<td>18</td>
<td>471</td>
</tr>
<tr>
<td>Stergiou et al16</td>
<td>119</td>
<td>636</td>
<td>211</td>
<td>3312</td>
</tr>
<tr>
<td>Tienchiou et al6</td>
<td>53</td>
<td>256</td>
<td>62</td>
<td>865</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>3484</td>
<td></td>
<td>11245</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>430</td>
<td></td>
<td>571</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2=9.59$, df=8 (P=0.29); P=17%
Test for overall effect: $Z=15.46$ (P=0.00001)

B

Mortality: masked HTN versus normotension

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Masked hypertension</th>
<th>Normotension</th>
<th>Odds ratio M-H, fixed, 95% CI</th>
<th>Odds ratio M-H, fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Booth et al26</td>
<td>29</td>
<td>385</td>
<td>15</td>
<td>353</td>
</tr>
<tr>
<td>Mancia et al29</td>
<td>25</td>
<td>184</td>
<td>43</td>
<td>909</td>
</tr>
<tr>
<td>Stergiou et al16</td>
<td>136</td>
<td>636</td>
<td>301</td>
<td>3312</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1205</td>
<td></td>
<td>4574</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>190</td>
<td></td>
<td>359</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2=1.76$, df=2 (P=0.41); P=0%
Test for overall effect: $Z=9.67$ (P=0.00001)

Figure 1: Masked HTN versus normotension – whole cohort.

Notes: (A) Composite cardiovascular events. (B) All-cause mortality.

Abbreviations: CI, confidence interval; HTN, hypertension; M–H, Mantel–Haenszel.
Comparison of Outcomes in Masked Uncontrolled (MUCH) vs. Controlled Hypertension

<table>
<thead>
<tr>
<th>Study name</th>
<th>Hazard ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OvA Study 2003</td>
<td>1.570</td>
<td>0.321</td>
<td>7.681</td>
<td>0.557</td>
<td>0.578</td>
</tr>
<tr>
<td>SHEAF Study 2004</td>
<td>2.060</td>
<td>1.221</td>
<td>3.474</td>
<td>2.710</td>
<td>0.007</td>
</tr>
<tr>
<td>Chieti-Pescara Study 2005-2017</td>
<td>2.010</td>
<td>1.449</td>
<td>2.788</td>
<td>4.181</td>
<td>0.000</td>
</tr>
<tr>
<td>IDACO Study 2005-2017</td>
<td>1.490</td>
<td>1.142</td>
<td>1.944</td>
<td>2.940</td>
<td>0.003</td>
</tr>
<tr>
<td>Hadassah Study 2006</td>
<td>1.375</td>
<td>0.787</td>
<td>2.400</td>
<td>1.120</td>
<td>0.263</td>
</tr>
<tr>
<td>J-HEALTH Study 2008</td>
<td>2.000</td>
<td>0.699</td>
<td>5.975</td>
<td>1.241</td>
<td>0.214</td>
</tr>
<tr>
<td>IDHOCO Study 2014</td>
<td>1.760</td>
<td>1.227</td>
<td>2.624</td>
<td>3.073</td>
<td>0.002</td>
</tr>
<tr>
<td>Dallas Heart Study 2015</td>
<td>2.845</td>
<td>1.566</td>
<td>5.167</td>
<td>3.434</td>
<td>0.001</td>
</tr>
<tr>
<td>Jackson Heart Study 2016</td>
<td>2.620</td>
<td>1.443</td>
<td>5.511</td>
<td>3.033</td>
<td>0.002</td>
</tr>
<tr>
<td>HONEST Study 2017</td>
<td>1.345</td>
<td>1.005</td>
<td>1.800</td>
<td>1.995</td>
<td>0.046</td>
</tr>
<tr>
<td>Spanish Registry Study 2018</td>
<td>2.030</td>
<td>1.669</td>
<td>2.469</td>
<td>7.091</td>
<td>0.000</td>
</tr>
<tr>
<td>Overall</td>
<td>1.796</td>
<td>1.566</td>
<td>2.061</td>
<td>8.371</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Q = 12.9, P = 0.2
I squared = 22.5
Tau squared = 0.01

Meta Analysis

Pierdomenico SD et al. Hypertens 2018; 72:862-869
Untreated and treated normotensive (NT) and masked hypertensive (MHT) nondiabetic subjects

Significant higher incidence of cardiovascular events in:
- Treated patients with MUCH versus treated patients with BP controlled
- Patients with MHT versus untreated normotensive patients

Fully adjusted hazard ratios (HR) for treated versus untreated MHTs are as follows: HR, 2.27 (95% confidence interval, 1.6–3.2; P<0.0001)
ABPM is more sensitive than HBPM in detecting Masked HTN

ABPM missed the detection of Masked HTN between 9-21% as detected by HBPM

HBPM missed the detection of Masked HTN 48-61% as detected by ABPM

Figure. Distribution of participants into categories based on the absence or presence of masked hypertension (MHT) on ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM).

Anstey DE et al. HTN 2018; 72:1200-1207
Detection of Masked Hypertension in Patients not on Drug Therapy

Office BP 120-129/<80 mm Hg after 3 months lifestyle modification; suspect MH

Daytime ABPM or HBPM BP ≥130/80 mm Hg

Yes

Masked Hypertension
Continue lifestyle modification and start antihypertensive therapy (Class IIa)

No

Elevated BP
• Lifestyle modification
• Annual ABPM or HBPM to detect MH (Class IIa)

ABPM = ambulatory BP monitoring; HBPM = home BP monitoring
Detection of Masked Uncontrolled Hypertension in Patients on Drug Therapy

- Office BP at Goal
  - Yes
  - CVD risk or Target Organ Damage
    - Yes
      - Screen for MUCH with HBPM (Class IIb)
        - HBPM above goal
          - Yes
            - MUCH: Intensify therapy (Class IIb)
          - No
            - Continue current therapy (Class IIa)
    - No
      - Screening not necessary (No benefit)
  - No
    - Continue current therapy (Class IIa)
Summary/Conclusions

• MH prevalence averages ~ 13% and up to 30% in some surveys.
• Prevalence of MH increases with higher (normal) office readings.
• Increased prevalence of MH is also seen in older persons, males, Blacks, and those with obesity, diabetes, CKD, and sleep apnea.
• Large longitudinal cohort studies show CVD risk is similar to that of sustained hypertension.
• Overlap between MH identified by HBPM and ABPM is only 60-75% though both show same CVD risk compared to NTH and sustained HTN.
• Likely due to the capability for nocturnal BP measurements, ABPM is more sensitive than HBPM for detecting MH.
• RCT data evaluating benefit of treatment is not yet available.
• Profiles of risk for treated patients showing MUCH parallel that of MH, respectively.