Assessing Blood Pressure for Clinical Research: Pearls & Pitfalls

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Objectives

• Review limitations of office (and research visit) measurements of BP
• Discuss the role of ABPM as the gold standard for accurate assessment & use of home BP monitoring as an alternative
• Describe pros & cons of each method
High blood pressure

• 1 out of 3 adults (74 million) in US
• 90% lifetime risk of developing hypertension
• Responsible for 35% of all myocardial infarctions and strokes and 50% of congestive heart failure
• Contributes to peripheral vascular disease, end-stage renal disease, aortic aneurysm, retinopathy

Relationship of BP to events

Treatment of high BP

- Reduces risk of strokes by 40%
- Reduces risk of MI by 25%
- Reduces risk of CHF by 50%

Burden of disease in 2010, for men and women combined

Lim et al. Lancet 2012;380:2224-2260
BP is commonly included in clinical research studies

- Studies of cardiovascular disease
- Studies involving kidneys, brain, heart,… just about any organ
- Drug studies, even drugs not for lowering BP (so-called cardiovascular effects of non-cardiovascular drugs)
- And it’s relatively “easy” to measure
Office BP

- BP measurement is basis for diagnosis (the most common diagnosis in adult primary care)
- Accurate measurement of BP is challenging, especially in busy office practices
- Mercury no longer used
- Oscillometric devices predominate
Limitations of Office BP

• Poor quality control due to technique
  – Wrong cuff size
  – Improper patient position (e.g. feet not on floor, arm not at heart level)
  – Failure to allow 5 minutes rest
  – If manual sphygmomanometer used
    • Letting air out of cuff too rapidly
    • Digit bias (rounding to nearest 5 or 10 mmHg)
    • Other observer biases
Why is a research visit BP better?

- Correct technique is followed
- Protocol is standardized
- Participant not there for a “doctor visit”

- Research BP measurements tend to be _______ than clinic (office) BP measurements
Limitation of clinic and research visit BP

Even when done correctly…

• Limited reliability due to the small number of readings

• Substantial variability from inherent and external factors
Misclassification

• Can overestimate usual BP
  – White-coat hypertension may be misclassified as (sustained) hypertension

• Overdiagnosis $\rightarrow$ overtreatment $\rightarrow$ harms
Lesser known…

But possibly more important

- Office reading may underestimate usual BP
- Person at increased cardiovascular risk not offered treatment
Alternatives to clinic or research visit BP

- Ambulatory BP monitoring
- Home BP monitoring
- Pharmacy kiosk monitoring
Pairing office & out-of-office

<table>
<thead>
<tr>
<th>ABPM (or HBPM)</th>
<th>Office BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>HTN</td>
<td>Masked</td>
</tr>
</tbody>
</table>

Office BP

- Normal
- HTN

ABPM

- Normal
- HTN

White Coat

Masked
Ambulatory BP monitoring

- Multiple readings over the course of 24 hours
- Superior to office BP in predicting outcomes
- Considered to be the noninvasive gold standard
Normal ABPM

- Systolic BP
- Diastolic BP
- Heart rate
- Nocturnal dip
- Morning surge

- Awake period
- Sleep time period
- Awake period
Definitions

• “Cut-offs” for ABPM:

<table>
<thead>
<tr>
<th></th>
<th>Cut-off (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awake average</td>
<td>135/85</td>
</tr>
<tr>
<td>Nighttime (sleep) average</td>
<td>120/70</td>
</tr>
<tr>
<td>24-hour average</td>
<td>130/80</td>
</tr>
</tbody>
</table>
BP dip and BP load

• Nocturnal dip
  – Normal is 10% to 20%
  – <10% is nondipper; >20% extreme dipper
  – Some are risers (reverse dippers)

• BP load
  – % of BP readings above threshold
  – <25% considered normal
  – >50% abnormal or higher risk
ABPM report

From 40+ BP measurements

- Mean overall BP
- Mean awake BP
- Mean sleep BP
- Nocturnal dip
- BP load

Lower if 1st two hours excluded
Graph of ABPM data

- Systolic BP
- Diastolic BP
- Nocturnal dip
- Heart rate

“White coat” period
Awake period
Sleep time period
Awake period
Graph of ABPM data

Nocturnal dip

Morning surge
ABPM Report

- **Quality**
  - 98% readings overall
- **Mean overall**: 138/85 mmHg
- **Mean awake**: 139/86 mmHg
- **Mean sleep**: 133/80 mmHg
- **Nocturnal dip**: 4%
- **SBP load**: 60%
Graph of ABPM data
ABPM Report

- Quality
  - 100% readings overall
- Mean overall BP: 142/84 mm Hg
- Mean awake BP: 148/89 mm Hg
- Mean sleep BP: 125/68 mm Hg
- Nocturnal dip: 15%/24%
- Systolic BP load: 74%
Predicting CVD outcomes

• “…systolic ABPM consistently and statistically significantly predicted stroke and other cardiovascular outcomes independently of office BP monitoring.”

Ann Intern Med. 2015 Feb 3;162(3):192-204.
Risk by ABPM

- N=1,332 in Japan; 10 years
- Risk by ABPM

<table>
<thead>
<tr>
<th>Condition</th>
<th>Death</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal BP</td>
<td>1.5</td>
<td>0.5</td>
</tr>
<tr>
<td>White Coat</td>
<td>1.5</td>
<td>1.0</td>
</tr>
<tr>
<td>Masked</td>
<td>1.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.0</td>
<td>3.0</td>
</tr>
</tbody>
</table>

- Normal BP
- White Coat
- Masked
- Hypertension
## Diagnostic accuracy of office BP

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Proportion Confirmed by 24-hr ABPM</th>
<th>95% CI</th>
<th>Screened, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kario, 1993</td>
<td>0.89</td>
<td>0.85-0.93</td>
<td>239</td>
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<tr>
<td>Inden, 1998</td>
<td>0.88</td>
<td>0.83-0.93</td>
<td></td>
</tr>
<tr>
<td>Pierdomenico, 1995</td>
<td>0.79</td>
<td>0.74-0.84</td>
<td>255</td>
</tr>
<tr>
<td>Khoury, 1992</td>
<td>0.52</td>
<td>0.43-0.60</td>
<td>131</td>
</tr>
<tr>
<td>Hozawa, 2002</td>
<td>0.35</td>
<td>0.27-0.42</td>
<td>150</td>
</tr>
<tr>
<td>First author, year</td>
<td>Proportion confirmed by daytime ABPM</td>
<td>95% CI</td>
<td>Screened, n</td>
</tr>
<tr>
<td>---------------------------</td>
<td>--------------------------------------</td>
<td>-------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Myers, 2010</td>
<td>0.93</td>
<td>0.87-0.99</td>
<td>69</td>
</tr>
<tr>
<td>Hond, 2003b</td>
<td>0.92</td>
<td>0.89-0.96</td>
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</tr>
<tr>
<td>Gustavsen, 2003</td>
<td>0.90</td>
<td>0.88-0.93</td>
<td>420</td>
</tr>
<tr>
<td>Zawadzka, 1998</td>
<td>0.86</td>
<td>0.83-0.90</td>
<td>410</td>
</tr>
<tr>
<td>Verdecchia, 1995</td>
<td>0.81</td>
<td>0.79-0.83</td>
<td>1333</td>
</tr>
<tr>
<td>Graves, 2010</td>
<td>0.78</td>
<td>0.73-0.81</td>
<td>313</td>
</tr>
<tr>
<td>Celis, 2002</td>
<td>0.78</td>
<td>0.68-0.80</td>
<td>419</td>
</tr>
<tr>
<td>Manning, 1999</td>
<td>0.77</td>
<td>0.73-0.81</td>
<td>186</td>
</tr>
<tr>
<td>Nasothimiou, 2012</td>
<td>0.77</td>
<td>0.73-0.81</td>
<td>361</td>
</tr>
<tr>
<td>Fogari, 1996</td>
<td>0.74</td>
<td>0.68-0.80</td>
<td>221</td>
</tr>
<tr>
<td>Ungar, 2004</td>
<td>0.74</td>
<td>0.70-0.78</td>
<td>388</td>
</tr>
<tr>
<td>Gerc, 2000</td>
<td>0.65</td>
<td>0.62-0.67</td>
<td>1466</td>
</tr>
<tr>
<td>Passanha, 2013</td>
<td>0.61</td>
<td>0.56-0.67</td>
<td>336</td>
</tr>
<tr>
<td>Martinez, 1999</td>
<td>0.61</td>
<td>0.55-0.66</td>
<td>345</td>
</tr>
<tr>
<td>Talleruphuus, 2006</td>
<td>0.54</td>
<td>0.44-0.63</td>
<td>108</td>
</tr>
<tr>
<td>Zabludowski, 1992</td>
<td>0.47</td>
<td>0.40-0.55</td>
<td>171</td>
</tr>
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Practical issues: pitfalls

- *ABPM not yet widely available*
  - Few providers/clinical staff trained
- Recommended during a work day
- Limits some physical activity
- While tolerable, it is inconvenient
- A session of insufficient readings is possible (which would necessitate repeat)
Tolerability

• Most bother is interference with normal sleeping pattern
  – 67% reported that the monitor woke them after falling asleep, and 8.6% removed it at some point during the night

• Adverse effects: discomfort (32%), skin irritation (37%), and bruising (7%)

Note that ABPM has other clinical indications

- Confirm hypertension in children
- Resistant hypertension
  - Up to a third of such patients have controlled ABP
- Labile hypertension
- Hypotensive episodes
- Postural hypotension
Keys to successful ABPM

• Patient preparation
• Clear communication about what to expect
• Proper fitting and instructions provided
• Our team has high success: in one study of repeated wearing, 408 out of 420 with quality data X2 sessions
Home BP monitoring

• Another method to obtain measurements outside the clinical setting
• Also better predictor of outcome than office BP
• Evidence base is growing, but not as strong
Home BP monitoring

- May be a more feasible method
- Widely available
- Relatively affordable (or could be loaned or given as a gift, particularly for research)
- Systematically performed, home BP averages correlate reasonably well with daytime ABPM average
Definitions

• “Cut-offs” for home BP monitoring:

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Home BP measurement protocol

• Have the patient commit to a minimum of five consecutive days of measurement
• Each day, patient takes 3 consecutive morning and 3 consecutive evening measurements
• Discard the first two days' measurements and the first measurement of each triplicate set of measurements
• Average the remaining measurements
Home BP monitoring pitfalls

• Misses large segments of day (and nocturnal)
• Relies on proper technique
• Dependent on patient effort / engagement
• Concerns over “trustworthiness” of data
Home BP monitoring: value beyond diagnosis

- Monitoring BP control
- Evaluating possible medication side effects
- Improving BP control (encouraging adherence)
HBPM should be taught

- MA or RA should review technique, frequency (may vary by purpose), recording of measurements
- Must make sure cuff size is correct
- Some research suggested patients selectively record or do not record BPs correctly
- Some equipped with memory and printer
Take away message

• While commonly used in research studies, office or clinic visit BP measurements may not provide accurate estimates of a person’s “true” BP

• Ambulatory BP monitoring is the best method for assessing BP, but is a mild inconvenience and may not be routinely available

• Home BP monitoring is another option for obtaining out-of-office measurements, but is limited by participant factors
Thank you for your attention!
If you want to learn more....

www.abpmcourse.com

• Morning didactic sessions
• Afternoon hands-on training
• Opportunities to evaluate monitors and software