Central Blood Pressure - Emerging Clinical Importance and Diagnostics

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25 years old male hypertensive came to clinic with BP-190/116 mm Hg. He had family history of hypertension. His ECG showed LVH. His central pressure monitoring showed evidence of severe arterial stiffness with increased augmentation index and pulse wave velocity. Which antihypertensive/s would be best for his current condition:

1. ACE inhibitor with calcium channel blocker
2. B-blocker with ACE inhibitor
3. Calcium channel blocker alone
4. Alfa blocker with Calcium channel blocker
5. Diuretic with ACE inhibitor
A 60 years old hypertensive patient underwent ABPM. His night time BP was noted to be higher than day time BP. What is this pattern and what is his cardiovascular risk status?

1. Normal dipping with increased risk
2. Excessive dipping with increased risk
3. Non-dipping with no risk
4. Reverse dipping with increased risk
5. 3+4
Q3

Carotid-femoral pulse wave velocity (PWV) is direct measurement and considered as the ‘gold-standard’ measurement of arterial stiffness.

A PWV measured by Syphgmo-Cor indicates increased arterial stiffness if

1. >10 M/S
2. 7-10 M/S
3. 5-7 M/S
4. <5 M/S
5. None of the above
What I would cover today

- Arterial Stiffness
- ASCOT and CAFÉ landmark studies
- Ways to measure of CASP
- Case scenario’s
- Dipping phenomenon
Arterial System

• The arterial system: large arteries and the arterioles

• The arterioles
  – act as taps
  – maintain steady flow to the tissues and organs

• The large arteries acts as **conduits** and **cushions**
Arterial System: Large arteries

- **Conduit**
  - Deliver blood with minimal fall in pressure to arterioles, as low resistance conduits.

- **Cushion**
  - Smooth out the pulsations imposed by the intermittently contracting heart.

- **Atherosclerosis**
  - narrowing of major artery
  - affect *conduit function* and cause ischemia or infarction of the tissue

- **Arteriosclerosis**
  - stiffening of major arteries eg. in hypertension and with aging
  - affect *cushioning function*
  - Increase cardiac load by increasing pulse pressure and systolic pressure
Arterial System: Conduit Function

• Arterial Flow
  – Imaging: US or angiogram
    • Degree of arterial narrowing or occlusion
    • Indirectly information of blood flow to tissue
  – Pressure measurement:
    • Brachial BP – systemic blood flow and perfusion
    • ABPI - overall functional flow to the lower limb
    • Difficult to measure in organs
  – Transcutaneous Oxygen measurement
    • Functional flow to the skin
Arterial System: Cushion Function

- **Arterial Wall Stiffness**
  - Recent years great emphasis has been placed on the role of *arterial stiffness* in the development of cardiovascular diseases
  
- **Assessment of arterial stiffness** is increasingly used in clinical assessment of patients
What is Arterial Waveform?

Reflects the status of the pump and state of the arterial tree.
# Pressure Wave

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Normal distensibility and normal pulse wave velocity (artery elastic → reflected wave comes in early diastole)</td>
</tr>
<tr>
<td>2.</td>
<td>Decreased distensibility but normal pulse wave velocity</td>
</tr>
<tr>
<td>3.</td>
<td>Decreased distensibility with increased pulse wave velocity (artery rigid → reflected wave comes in systole with increase in pulse wave velocity)</td>
</tr>
</tbody>
</table>
Wave form analysis

- P1 peak of outgoing pressure wave
- SP Central aortic systolic pressure (CASP)
- DP Central aortic diastolic pressure
- ΔP augmentation PP pulse pressure
- Alx augmentation index

Figure 2. Hemodynamic parameters derived by pulse wave analysis of the central aortic pressure wave. T0 indicates the time at the start of the waveform; T1, duration from start of waveform to the first peak/shoulder (outgoing pressure wave); T2, duration from start of waveform to the second peak/shoulder (reflected pressure wave); ED, ejection duration, or duration from start of waveform to closure of the aortic valve (incisura); SP, central aortic systolic pressure; DP, central aortic diastolic pressure; P1, P1 height difference between the minimum pressure and the pressure at the first peak/shoulder (T1); augmentation (ΔP), difference between maximal pressure (central aortic systolic pressure) and pressure at the first peak/shoulder (P1 height); PP, pulse pressure; and Alx, augmentation index.
<table>
<thead>
<tr>
<th></th>
<th>Normal Aorta (Young Adults)</th>
<th>Stiff Aorta (Older Adults)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Aortic BP (mm Hg)</td>
<td>130 Systolic 80 Diastolic</td>
<td>140</td>
</tr>
<tr>
<td>2. PWV (m/s)</td>
<td>5.0</td>
<td>10.0</td>
</tr>
<tr>
<td>3. Reflected Wave Early Diastole</td>
<td></td>
<td>Late Systole</td>
</tr>
<tr>
<td>4. Pulse Wave Shape</td>
<td>![Pulse Wave Graph]</td>
<td></td>
</tr>
<tr>
<td>5. Aortic BP (mm Hg)</td>
<td>130 Systolic 80 Diastolic</td>
<td>160</td>
</tr>
</tbody>
</table>
Pulse Wave Velocity

• European Hypertension Guidelines 2014

• PWV measurement
  – Accepted as the most simple, non-invasive, robust and reproducible method to determine arterial stiffness

• Carotid-femoral PWV (>10 m/s indicates arterial stiffness)
  – Direct measurement
  – Considered as the ‘gold-standard’ measurement of arterial stiffness
Blood Pressure and Central Aortic Pressure

• Brachial blood pressure is a standard way of recording blood pressure

• It is strong predictor of clinical outcomes in people with hypertension

• It is assumed that brachial blood pressure accurately reflects pressures in the central aorta and thus left ventricular load
### ASCOT STUDY

| Patients’ key clinical characteristics | Hypertensive patients 19257 with >= 3 CV risk factors  
No previous MI/CHD |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental Regimen</td>
<td>Amlodipine arm</td>
</tr>
<tr>
<td>Control Regimen</td>
<td>Atenolol arm</td>
</tr>
<tr>
<td>Followup</td>
<td>5 years</td>
</tr>
<tr>
<td>Primary outcome</td>
<td>Nonfatal MI and fatal CHD</td>
</tr>
</tbody>
</table>
ASCOT: Systolic and diastolic blood pressure

SBP

Mean difference 2.7

164.1
163.9
137.7
136.1

DBP

Mean difference 1.9

94.8
94.5
79.2
77.4
ASCOT: Summary of all end points

Unadjusted Hazard ratio (95% CI)

0.90 (0.79-1.02)

0.87 (0.76-1.00)

0.87 (0.79-0.96)

0.84 (0.78-0.96)

0.89 (0.81-0.99)

0.76 (0.65-0.90)

0.77 (0.66-0.89)

0.84 (0.66-1.05)

1.27 (0.80-2.00)

0.68 (0.51-0.92)

0.98 (0.81-1.19)

0.65 (0.52-0.81)

1.07 (0.62-1.85)

0.70 (0.63-0.78)

0.85 (0.75-0.97)

0.86 (0.77-0.96)

0.84 (0.76-0.92)

Primary
Non-fatal MI (incl silent) + fatal CHD

Secondary
Non-fatal MI (exc. Silent) + fatal CHD
Total coronary end point
Total CV event and procedures
All-cause mortality
Cardiovascular mortality
Fatal and non-fatal stroke
Fatal and non-fatal heart failure

Tertiary
Silent MI
Unstable angina
Chronic stable angina
Peripheral arterial disease
Life-threatening arrhythmias
New-onset diabetes mellitus
New-onset renal impairment

Post hoc
Primary end point + coronary revasc procs
CV death + MI + stroke

The area of the blue square is proportional to the amount of statistical information.
CAFE Study Design

• Large sub-study of ASCOT study

• 2199 subjects recruited from 5 UK ASCOT centres (UK, Ireland) 19257 subjects in ASCOT study

• Recruitment into CAFE commenced when patients were stable after up-titration of ASCOT medication (~1 year after start of ASCOT)
Primary Objective

• The different blood pressure–lowering regimens in ASCOT (atenolol versus amlodipine arm) would produce different effects on central aortic pressures and haemodynamics despite similar effects on brachial blood pressure

Secondary Objective

• Central aortic pressures would be an important determinant of clinical outcomes
Brachial and Central Aortic Systolic Blood Pressure
(± 95% CI)

Brachial SBP
Diff Mean (AUC) = 0.7 (-0.4, 1.7) mm Hg

Central SBP
Diff Mean (AUC) = 4.3 (3.3, 5.4) mm Hg

Atenolol
Amlodipine

<table>
<thead>
<tr>
<th>Time (Years)</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>133.9</td>
</tr>
<tr>
<td>0.5</td>
<td>133.2</td>
</tr>
<tr>
<td>1</td>
<td>133.2</td>
</tr>
<tr>
<td>1.5</td>
<td>125.5</td>
</tr>
<tr>
<td>2</td>
<td>121.2</td>
</tr>
</tbody>
</table>

P = 0.07

P < 0.0001

Circulation. 2006;113:1213-1225
CAFE Study Conclusions

• Central aortic pressure is an important independent determinant of clinical outcomes

• Results of the CAFE study suggest that the “central aortic blood pressure hypothesis” is a plausible mechanism to explain the better clinical outcomes for hypertensive patients treated with amlodipine ± perindopril-based therapy in ASCOT
Questions

• Can we measure CASP, Augmentation index and pulse wave velocity?

• Can it be non-invasive?

• Is it accurate if measured non-invasively?
Radial Artery Pulse Wave Analysis

• Obtain radial artery waveform by applying applanation tonometry (using Milar tonometer)

• Radial artery waveform was calibrated to the average brachial blood pressure measurement of patient

• Corresponding central aortic pressure waveform derived using generalised transfer function (SphymoCor version 7)
Pulse Wave Analysis

Sensor

Artery

Bone

Brachial Blood Pressure

Transfer function

Radial

Central Aortic

Central Aortic
Step 1

The brachial blood pressure should be taken just prior to performing the SphygmoCor measurement, to allow for calibration of the radial pressure waveform.
Step 2

The tonometer (pressure sensor) is placed on the wrist directly above the radial artery, at the location where the operator feels the strongest signal from the pulse.

It is important the tonometer is placed correctly to ensure a strong, steady and reproducible pressure signal (Operator index >80%)
Pulse Wave Velocity (m/s): 7.8 ± 0.5
Wrist BP measurement for pulse wave analysis/ CASP and 24 hours ABPM
# Case

## Summary

<table>
<thead>
<tr>
<th>Start</th>
<th>Date: 13-Aug-2007</th>
<th>Time: 09:35</th>
</tr>
</thead>
<tbody>
<tr>
<td>End</td>
<td>Date: 14-Aug-2007</td>
<td>Time: 09:20</td>
</tr>
</tbody>
</table>

**Calibration Values:**
- **Systolic:** 174 mmHg
- **Diastolic:** 79 mmHg

**Systolic Pressure Load:**
- **Daytime:** 100.0%
- **Nighttime:** 100.0%

### Systolic / Diastolic

<table>
<thead>
<tr>
<th>Systolic / Diastolic</th>
<th>mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ave. 24-hr BP (PP)</td>
<td>173 / 81 (92)</td>
</tr>
<tr>
<td>Ave. Day BP (PP)</td>
<td>175 / 82 (93)</td>
</tr>
<tr>
<td>Ave. Night BP (PP)</td>
<td>168 / 79 (89)</td>
</tr>
<tr>
<td>% Dip</td>
<td>4.0% / -</td>
</tr>
<tr>
<td>Max. Systolic (Time)</td>
<td>203 (08:50)</td>
</tr>
<tr>
<td>Min. Systolic (Time)</td>
<td>154 (00:20)</td>
</tr>
</tbody>
</table>

**Reference Values for Dipper Status**

<table>
<thead>
<tr>
<th>% Dip</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0%</td>
<td>Reverse Dipper</td>
</tr>
<tr>
<td>0% to 10%</td>
<td>Non-Dipper</td>
</tr>
<tr>
<td>10% to 15%</td>
<td>Normal Dipper</td>
</tr>
<tr>
<td>&gt; 15%</td>
<td>Extreme Dipper</td>
</tr>
</tbody>
</table>

**Calculation:**

\[
\text{% Dip} = \left( \frac{\text{Ave. Day Systolic BP} - \text{Ave. Night Systolic BP}}{\text{Ave. Day Systolic BP}} \right) \times 100\%
\]
### TABLE 6. Definitions of hypertension by office and out-of-office blood pressure levels

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic BP (mmHg)</th>
<th>Diastolic BP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office BP</td>
<td>≥140</td>
<td>and/or ≥90</td>
</tr>
<tr>
<td>Ambulatory BP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daytime (or awake)</td>
<td>≥135</td>
<td>and/or ≥85</td>
</tr>
<tr>
<td>Nighttime (or asleep)</td>
<td>≥120</td>
<td>and/or ≥70</td>
</tr>
<tr>
<td>24-h</td>
<td>≥130</td>
<td>and/or ≥80</td>
</tr>
<tr>
<td>Home BP</td>
<td>≥135</td>
<td>and/or ≥85</td>
</tr>
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</table>

BP, blood pressure.

ESH hypertension guidelines 2013
### Reference Values for Dipper Status

<table>
<thead>
<tr>
<th>Percentage Range</th>
<th>Status</th>
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<tbody>
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\% \text{ Dip} = \left( \frac{\text{Ave. Day Systolic BP} - \text{Ave. Night Systolic BP}}{\text{Ave. Day Systolic BP}} \right) \times 100\%
\]
Risks associated with non-dipping or reverse dipping

• Nondipping is a risk factor for the development of LVH, heart failure, and other cardiovascular complications
  - J Hypertens. 2010;28(10):2036

• Nondipping has also been associated with moderately increased albuminuria (formerly called "microalbuminuria") and more rapid progression of nephropathy in patients with diabetes mellitus
  - Nephrol Dial Transplant. 1998;13(9):2257
Mechanisms of Non–dipping

• The underlying mechanisms of nondipping are unknown, but intrinsic renal defects may contribute
  • Transplantation. 1995;59(9):1270.

• There is also some evidence suggesting that melatonin plays a role.

• Melatonin reduces night blood pressure in patients with nocturnal hypertension.
  • Am J Cardiol. 1999;83(9):1417.
Conditions associated with non-dipping phenomenon

- Sleep disturbance
- Obstructive sleep apnoea, obesity
- High salt intake in salt-sensitive subjects
- Orthostatic hypotension, autonomic dysfunction
- Chronic kidney disease (CKD), diabetic neuropathy
- Old age
Q1

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Take home message

• Measures of Arterial stiffness
• Central BP Vs peripheral BP
• Augmentation index
• Landmark studies – ASCOT and CAFÉ
• Ways to measure central BP, arterial stiffness
• Dipping phenomenon
• Normal dippers, Non-dippers/ reverse dippers and extreme dippers and relation to cardiovascular mortality
Thank you for your time and attention