Ασθενής 35 ετών με φλεβοκομβική ταχυκαρδία και αρτηριακή πίεση ιατρείου 160/100 mmHg. Ποια η διαγνωστική και θεραπευτική προσέγγιση;

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The case

• a 35 year-old male was referred to the Hypertension Unit for blood pressure evaluation because of measurements of increased Systolic/Diastolic BP

Personal Hx and patient profile:
• Moderate smoking
• Physically active
• BMI: 29Kg/m²
# Blood pressure evaluation

<table>
<thead>
<tr>
<th>1&lt;sup&gt;st&lt;/sup&gt; visit</th>
<th>Left</th>
<th>Right</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt;</td>
<td>165/104</td>
<td>159/95</td>
<td>102</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt;</td>
<td>158/97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt;</td>
<td>162/102</td>
<td>160/100mmHg</td>
<td>108</td>
</tr>
<tr>
<td>Standing</td>
<td>165/96</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Grade II HTN
- High HR
Office BP measurement: The technique

- Seated comfortably for **5 minutes**
- **Three BP** measurements should be recorded, 1–2 min apart, and **additional measurements only if the first two readings differ by >10 mmHg.**
- BP is recorded as the average of the last two BP readings.
- Korotkoff sounds I and V
- Measure both arms and **use arm with higher BP**
- 1 and 3 minutes in standing position
- Record heart rate and use pulse palpation to exclude arrhythmia
Measuring heart rate in the clinic

1. **Exercise, smoking, alcohol and coffee** consumption should be avoided before measurement.
2. The patient should be allowed to **relax for at least 5min**.
3. **Background noise and talking** should be avoided.
4. **Room temperature** should be comfortable.
5. **The sitting position** should be preferred.
6. The individual should be comfortably seated with **legs uncrossed**.
7. HR should be measured by **pulse palpation over a 30-s period**.
8. Electrocardiographic measurement is **acceptable but not recommended**.
9. HR should be measured **after each blood pressure reading**.
10. **At least two measurements should be taken and averaged out**.

Patient evaluation plan

**BP**
- Office BP and HTN confirmation

**Clinical evaluation**
- Clinical
- Physical
- Routine Lab
- 2ndary HTN

**HMOD-Basic**
- ECG
- ACR
- eGFR
- Fundoscopy

**HMOD-Advanced**
- Echo
- Carotids
- Abdominal US
- PWV
- ABI
- Brain

**CV Risk**
- Age
- RFs
- HMOD

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Checkpoint 1: Diagnosis of hypertension

- **Optimal BP <120/80**: Repeat BP at least every 5 years
- **Normal BP 120-129/80-84**: Repeat BP at least every 3 years
- **High-normal BP 130-139/85-89**: Repeat BP at least annually
- **Hypertension ≥140/90**: Consider masked hypertension
  - Use either to confirm diagnosis
  - Repeated visits for office BP measurement
  - Out-of-office BP measurement (ABPM or HBPM)

Indications for ABPM or HBPM see Table 11

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Checkpoint 2: Evaluating risk

Moderate risk

People with:
- A calculated 10 year SCORE of ≥1 to <5%
- Grade 2 hypertension
- Many middle-aged people belong to this category

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**Checkpoint 3: Secondary hypertension in this patient?**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger patients (&lt;40 years) with grade 2 hypertension or onset of any grade of hypertension in childhood</td>
<td></td>
</tr>
<tr>
<td>Acute worsening hypertension in patients with previously documented chronically stable normotension</td>
<td></td>
</tr>
<tr>
<td>Resistant hypertension (see section 8.1)</td>
<td></td>
</tr>
<tr>
<td>Severe (grade 3) hypertension or a hypertension emergency (see section 8.3)</td>
<td></td>
</tr>
<tr>
<td>Presence of extensive HMOD</td>
<td></td>
</tr>
<tr>
<td>Clinical or biochemical features suggestive of endocrine causes of hypertension or CKD</td>
<td></td>
</tr>
<tr>
<td>Clinical features suggestive of obstructive sleep apnoea</td>
<td></td>
</tr>
<tr>
<td>Symptoms suggestive of phaeochromocytoma or family history of phaeochromocytoma</td>
<td></td>
</tr>
</tbody>
</table>

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Secondary hypertension by age group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Range (%)</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young adults (19–40 years)</td>
<td>5–10</td>
<td>- Renal parenchymal disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Fibromuscular dysplasia (especially in women)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Undiagnosed monogenic disorders</td>
</tr>
<tr>
<td>Middle-aged adults (41–65 years)</td>
<td>5–15</td>
<td>- Primary aldosteronism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Obstructive sleep apnoea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Cushing’s syndrome</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Phaeochromocytoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Renal parenchymal disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Atherosclerotic renovascular disease</td>
</tr>
</tbody>
</table>

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Tachycardia in the hypertensive patient: A differential diagnosis when he/she is young

- Drugs & recreational agents
- OSA
- Thyroid disease
- Pheochromocytoma
- Other rare causes (FMD, Cushing, Monogenic HTN etc)

<table>
<thead>
<tr>
<th>Table 8 Causes of physiological sinus tachycardia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiological causes</td>
</tr>
<tr>
<td>Pathological causes</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Drugs</td>
</tr>
<tr>
<td>Recreational agents</td>
</tr>
<tr>
<td>Illicit drugs</td>
</tr>
</tbody>
</table>
Drugs?
## Drugs affecting BP and inducing tachycardia

<table>
<thead>
<tr>
<th>Class</th>
<th>Drugs</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sympathomimetic agents</td>
<td>Anphetamines (dextroamphetamine, methamphetamine, methylphenidate; phenylpropanolamine, ephedrine, pseudoephedrine)</td>
<td>Cause dose-related increases in blood pressure; CNS stimulant</td>
</tr>
<tr>
<td>NSAIDs and COX-2 inhibitors</td>
<td>Ibuprofen, diclofenac, celecoxib</td>
<td>Block COX-1 and COX-2 enzymes, which leads to a reduction in prostaglandin formation; cause dose-related increases in sodium and water retention</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Prednisone, hydrocortisone, hydrocortisone</td>
<td>Cause sodium retention, resulting in dose-related fluid retention</td>
</tr>
<tr>
<td>CNS stimulants</td>
<td>Caffeine</td>
<td>Stimulant effect</td>
</tr>
<tr>
<td>Estrogens and progestins</td>
<td>Oral contraceptives, ERT/HRT</td>
<td>Estrogen stimulates the hepatic production of the renin substrate angiotensinogen; both appear to contribute in a dose-dependent fashion</td>
</tr>
<tr>
<td>Dietary supplements</td>
<td>Ginseng, natural licorice, yohimbine</td>
<td>Mild stimulant effect; increase arterial pressure</td>
</tr>
<tr>
<td>SNRIs</td>
<td>Venlafaxine, sibutramine</td>
<td>Increase levels of noradrenaline and the subsequent potentiation of noradrenergic neurotransmission</td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>Cyclosporine, tacrolimus</td>
<td>Increase prostaglandin synthesis and decrease water, sodium, and potassium excretion</td>
</tr>
</tbody>
</table>
The young patient with hypertension in the doping era

- Anabolic steroids
- Growth hormone
- Insulin-like GFs
- Selective androgen receptor modulators
- hCG
- EPO
- Peptide hormones
- B-2 agonists
- Amphetamines

- LVH
- Diastolic dysfunction
- Subclinical systolic dysfunction
- Fibrosis
- No reversal of LVH after activity cessation
- Coronary artery disease
Hyperthyroidism
Hyperthyroidism

**Prevalence:** 1-2%

**Symptoms:** Palpitations, weight loss, anxiety, heat intolerance

**HTN:** More often systolic

**Clinical:** Tachycardia, AF, exophthalmus

**Screening:** TSH

**Lab:** fT4 and/or fT3 increased
Obstructive Sleep Apnea?
Acute effect of an apneic event

- Cessation of airflow
- O₂ desaturation and CO₂ retention
- Increasing stimulation of peripheral/central chemoreceptors
  - Apnea-induced cessation of pulmonary stretch receptor inhibition of central SNS outflow
- Increased sympathetic discharge (that persists during the day)
- Vasoconstriction that counteracts Mueller manoeuvre to maintain BP
- Arousal, resumption of breathing
- Tachycardia, increased CO, BP surge

Assessing for sleep apnea

EPWORTH

1. Fatigue during the daytime
2. Difficulty concentrating
3. Excessive daytime sleepiness
4. Work or school performance issues
5. Insomnia

EPWORTH is a tool used to assess the risk of sleep apnea. It is based on the Berlin Questionnaire.
Neck circumference

- men: >43 cm
- women: >37 cm
## Portable monitoring devices

<table>
<thead>
<tr>
<th>Type 2</th>
<th>Comprehensive Portable (PSG at home)</th>
<th>Minimum of 7 channels, including EEG, EOG, chin EM, ECG or HR, airflow, respiratory effort, and SpO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 3</td>
<td>Modified Portable Sleep ApneaTesting (No sleep stages)</td>
<td>Minimum of 4 channels monitored, including ventilation or airflow (at least 2 channels of respiratory movement, or respiratory movement and airflow), heart rate or ECG and SpO2</td>
</tr>
<tr>
<td>Type 4</td>
<td>Continuous Single or Dual Bioparameters</td>
<td>One or 2 channels, typically including oxygen saturation or airflow</td>
</tr>
</tbody>
</table>

- For patients with high pretest probability for moderate-severe OSA
- For immobile, critically ill patients
- Not in comorbid conditions (e.g. COPD)
- Not for screening in general population
Pheochromocytoma
✓ **Pheochromocytoma**: Tumor arising from adrenomedullary chromaffin cells that commonly produces one or more catecholamine.

✓ **Paraganglioma**: Tumor derived from extra-adrenal chromaffin cells of the sympathetic paravertebral ganglia of thorax, abdomen, and pelvis.

✓ **Paragangliomas of parasympathetic origin** are usually located in the head and neck region, rarely synthesize catecholamines, and are chromaffin negative.

- **Prevalence in HTN**: 0.2-0.5%
- **15-30%**: Genetic
- **5-10%**: Malignant
- **Pheochromocytomas** (80-85%)
- **Paragangliomas** (15-20%)

- Adrenals
- Abdomen
- Thorax
Pheochromocytoma: Clinical

- **Paroxysmal HTN**
- **Palpitation**
- **Perspiration**
- **Pallor**
- **Pounding Headache**

Sustained HTN (50%)
Paroxysms (25%)
Crisis & sustained HTN (25%)
Labile and orthostatic hypotension

Hyperadrenergic Syndrome (5 Ps)

PCC Crisis

Palpitations, headache, sweating, anxiety, tremor, nausea, vomiting, abdominal pain

PCC

Weight loss
Heat inotolerance

BP

Hypermetabolism

Hyperadrenergic Syndrome

BP

PCC

Hypermetabolism
PCC and genetic syndromes

NF Type I

vHL
PCC: Lab tests following clinical suspicion

- Plasma metanephrines
- 24 hour urine metanephrines, normetanephrine,
- Plasma and urine catecholamines
- VMA, Neuropeptide Y
- Chromogranin A
PCC: Imaging
Lateralization: 123-I-MIBG

- Secure diagnosis and identify metastasis
- Sens: 80-95%
- Spec: 95-100%
And what if all tests are negative?
So, what is tachycardia?

✓ >100bpm is the standard
✓ No normal distribution
✓ Cardiovascular risk increases at well lower heart rate levels
✓ Most studies identify a higher risk at 75-85bpm
✓ About 30% of hypertensives have a heart rate >80bpm

NHANES data, 2011
Heart rate: marker or risk factor?

- ↑ SNS
- ↓ Diastolic time
- Low shear stress
- ↑ Arterial mechanical stress
- ↑ Stiffness
- ↑ CardiacO2 consumption
- BP
- Obesity
- Hyperinsulinemia
- Dyslipidemia
- Atherosclerosis development and plaque progression
- ↓ Diastolic time
- Low shear stress
- ↑ Arterial mechanical stress
- ↑ Stiffness
- ↑ CardiacO2 consumption
- BP
- Obesity
- Hyperinsulinemia
- Dyslipidemia
- Atherosclerosis development and plaque progression
Evaluating risk

<table>
<thead>
<tr>
<th>Demographic characteristics and laboratory parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (men &gt; women)</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Smoking (current or past history)</td>
</tr>
<tr>
<td>Total cholesterol and HDL-C</td>
</tr>
<tr>
<td>Uric acid</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Overweight or obesity</td>
</tr>
<tr>
<td>Family history of premature CVD (men aged &lt;55 years and women aged &lt;65 years)</td>
</tr>
<tr>
<td>Family or parental history of early-onset hypertension</td>
</tr>
<tr>
<td>Early-onset menopause</td>
</tr>
<tr>
<td>Sedentary lifestyle</td>
</tr>
<tr>
<td>Psychosocial and socioeconomic factors</td>
</tr>
<tr>
<td>Heart rate (resting values &gt;80 beats/min)</td>
</tr>
</tbody>
</table>

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Heart rate and CV events among hypertensives

- 15193 patients of the VALUE trial
- Heart rate measured by ECG
- In-treatment heart rate consistently associated with cardiac events independently of BP control

Julius S et al. Am J Cardiol 2012
Treating the patient

- High normal BP
  BP 130-139/85-89 mmHg
  - Lifestyle advice
  - Consider drug treatment in very high risk patients with CVD, especially CAD

- Grade 1 Hypertension
  BP 140-159/90-99 mmHg
  - Lifestyle advice
  - Immediate drug treatment in high or very high risk patients with CVD, renal disease or HMOD
  - Drug treatment in low moderate risk patients without CVD, renal disease or HMOD after 3-6 months of lifestyle intervention if BP not controlled

- Grade 2 Hypertension
  BP 160-179/100-109 mmHg
  - Lifestyle advice
  - Immediate drug treatment in all patients
  - Aim for BP control within 3 months

- Grade 3 Hypertension
  BP ≥180/110 mmHg
  - Lifestyle advice
  - Immediate drug treatment in all patients
  - Aim for BP control within 3 months

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Treating the patient: Lifestyle changes

✓ Quit smoking
✓ Reduce alcohol
✓ Reduce coffee
✓ Control weight
✓ Moderate exercise
Treatment

1 Pill
Initial therapy
Dual combination
ACEi or ARB + CCB or diuretic

1 Pill
Step 2
Triple combination
ACEi or ARB + CCB + diuretic

2 Pills
Step 3
Triple combination + spironolactone or other drug
Resistant hypertension
Add spironolactone (25-50 mg o.d.) or other diuretic, alpha-blocker or beta-blocker

Consider monotherapy in low risk grade 1 hypertension (systolic BP <150mmHg), or in very old (≥80 years) or frail patients

Consider referral to a specialist centre for further investigation

Beta-blockers
Consider beta-blockers at any treatment step, when there is a specific indication for their use, e.g. heart failure, angina, post-MI, atrial fibrillation, or younger women with, or planning, pregnancy

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Benefit from heart-rate reduction?

**Clear benefit**
- Heart failure
- Post-MI

**Hypertensives?**
- No prospective data
- Only retrospective (yet positive) data

[Image]
Conclusions

• Young patients with hypertension and resting tachycardia should undergo diligent examination to ascertain the above findings.

• Specific causes of secondary hypertension are intrinsically accompanied by tachycardia.

• Most of these can be easily ruled out with physical and basic laboratory exams.

• Although tachycardia is a marker of risk, due to lack of evidence there is no clear indication for selective reduction of heart rate in the absence of symptoms or specific diagnosis.