



V.N. Karazin Kharkov National University
Medical School
Department of Internal Medicine

Passions around Pheochromocytoma

Speakers: 6th course students Abiodun M.A, Adegoke E.A, Aduroja A.O

Adviser: ass. prof. Petrenko E.V., prof. Yabluchansky N.I.

Arterial Hypertension: Definition

- A systolic blood pressure (**SBP**) **>139 mmHg**
and/or
- A diastolic (**DBP**) **>89 mmHg**.
- Based on the average of **two or more** properly measured, seated BP readings
- On each of **two or more** office visits
or
- By virtue of the patient taking antihypertensive medications

Classification of office BP levels (mmHg)*

Category	Systolic		Diastolic
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90

* The blood pressure (BP) category is defined by the highest level of BP, whether systolic or diastolic. Isolated systolic hypertension should be graded 1, 2, or 3 according to systolic BP values in the ranges indicated.

AH stages (WHO-ISH, 1993)

Stage	Signs
I	No objective signs of organic changes
II	At least one of the following signs of organ damage: <ul style="list-style-type: none">- Left ventricular hypertrophy (x-ray film, electrocardiogram, echocardiogram)- Generalized or focal narrowing of retinal masses- Proteinuria or slightly raised plasma levels of creatinine concentrations (106- 107 $\mu\text{mol/l}$), or both- Ultrasound or radiological evidence of atherosclerotic plaque (carotid arteries, aorta, iliac, and femoral arteries)
III	Both symptoms and signs have appeared as a result of end organ damage including: <ul style="list-style-type: none">- Heart: angina pectoris, myocardial infarction, heart failure- Brain: transient ischaemic attack, stroke, hypertensive encephalopathy- Optic fundi: retinal haemorrhages and exudates with or without papilloedema- Kidney: plasma creatinine concentration $>177 \mu\text{mol/l}$, renal failure- Vessels: dissecting aneurysm, symptomatic arterial occlusive disease

Primary AH

- also known as essential AH
- accounts for 95% cases of AH
- no universally established cause known

Secondary AH

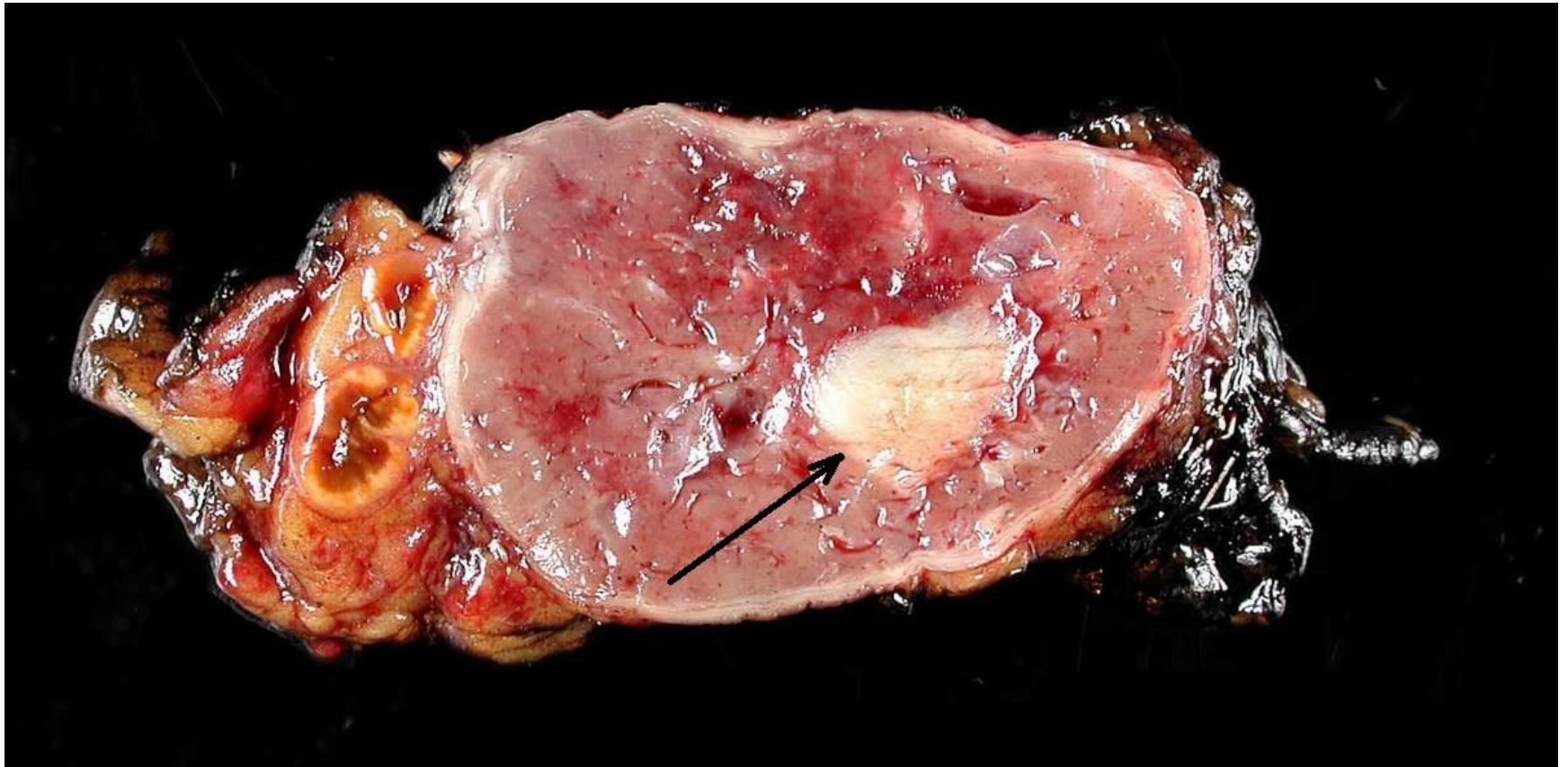
- less common cause of AH(5%)
- secondary to other potentially rectifiable causes

Secondary arterial hypertension

Renal parenchymal hypertension	Pheochromocytoma	Aortic coarctation
Renovascular hypertension	Hypothyroidism	Brainstem vascular compression
Primary aldosteronism	Hyperthyroidism	Sleep apnea syndrome
Cushing's syndrome	Hyperparathyroidism	Drug-induced hypertension

Pheochromocytoma

adrenal tumor of the medulla that arise from chromaffin cells in origin, associated with hypertension and abnormal glucose tolerance due to catecholamine excess.



Gross pathology showing a pheochromocytoma in the adrenal medulla

Pheochromocytoma

- Pheochromocytomas are rare, reportedly occurring in 0.05–0.2% of hypertensive individuals. This accounts for only a portion of cases, however, as patients may be completely asymptomatic.
- A retrospective study from the Mayo Clinic revealed that in 50% of cases of pheochromocytoma, the diagnosis was made at autopsy.
- Approximately 10% of pheochromocytomas are discovered incidentally.

Pheochromocytoma

Classically, pheochromocytoma manifests as spells with the following 4 characteristics:

- Headaches
- Palpitations
- Diaphoresis
- Severe hypertension

Typical patterns of the spells are as follows:

- Frequency may vary from monthly to several times per day
- Duration may vary from seconds to hours
- Over time, spells tend to occur more frequently and become more severe as the tumor grows

Pheochromocytoma

- Biochemical testing via measurement of plasma free metanephrines or urinary fractionated metanephrines should be performed in patients suspected of having pheochromocytoma.
- Computed tomography (CT), rather than magnetic resonance imaging (MRI), is recommended as the first-line imaging technique.

Lenders JW, Duh QY, Eisenhofer G, Gimenez-Roqueplo AP, Grebe SK, Murad MH, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2014 Jun. 99(6):1915-42.

- Patients should be referred to specialists if a high blood catecholamine level, high metanephrine or normetanephrine level (corrected for creatinine) in a spot urine sample (>300 ng/mg Cr) or adrenal incidentaloma is noted.

The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2009). *Hypertens Res* 2009; 32: 3107.

OUR PATIENT

- Name: T.D.V.
- Sex: Male
- Age: 37 Years
- Location: Kharkiv
- Occupation: Security officer
- The name of referral institution: self-appeal
- Date of first visit: 03.11.2015
- Patient was treated as outpatient

COMPLAINTS

- Increased blood pressure, tachycardia episodes, sometimes headaches of pulsating character after trainings at the gym
- No sweating, weight loss, or postural hypotension

Anamnesis Morbi

- Started monitoring himself with a home blood pressure monitor at the age of 25 after the diagnosis of his mother with pheochromocytoma. BP readings did not exceed 140/90 mm Hg. Since the age of 30 there were episodes of tachycardia and headaches after training in the gym. BP levels periodically increased up to 160/100 mm Hg, also at rest, without any accompanying symptoms. In 2014 was examined in National Institute of Therapy named by L.T. Malaya, where the diagnosis was made: Essential Arterial Hypertension, II st., with sympathetic-adrenal paroxysms. Normatens 1 tablet at bedtime and carvedilol 12,5 mg 2 times daily under HR control were recommended.
- Despite this, patient believes that pheochromocytoma can be the cause of his complaints.
- Presently episodically takes Normatens (when SBP \geq 160) and Koriol (carvedilol) in case of tachicardia. Last 2 months didn't take any medications.

Anamnesis Vitae

- Professional wrestler in the past
- Works as security officer
- Smokes approximately 12 cigarettes per day.
- Feeds regularly and adequately
- Three times a week has a training in the gym
- Denied drug usage and alcohol intake
- Father died of sudden cardiac death at age 54
- Mother was diagnosed with pheochromocytoma, not operated

Status Presence Objectivus

- Condition is satisfactory, clear consciousness, active and not in distress
- Hypersthenic type of body constitution
- Height-168 cm, weight - 78 kg, BMI= 27.6 kg/m²
- Skin – normal pink color
- Peripheral lymph nodes: not palpable
- Thyroid lobes are not palpable, the isthmus is palpated as a homogeneous smooth cross-strand, 1 cm wide
- Musculoskeletal system examination unremarkable
- Lungs: resonance percussion note, vesicular breathing over the lungs fields, RR 18 bpm
- Heart borders are not extended, heart activity is rhythmic with HR of 72 bpm. Heart tones are clear in all auscultating points.
- Blood pressure sin 145/100 mm Hg, dex 150/105 mm Hg
- Abdomen of normal size, painless in palpation. Liver at the costal margin, painless. Absence of vascular sounds during abdomen auscultation.
- Pasternatskiy sign is negative on both sides
- No peripheral edema

PLAN OF SURVEY

- Full blood count
- Urinalysis
- Biochemical panel
- ECG
- EchoCG
- ABPM
- Abdominal ultrasound
- Plasma metanephrine testing
- CT scanning of the kidney, adrenal glands

Full blood count

Options	Results	NR
Hemoglobin	156	130,0 – 160,0 g/L
Erythrocytes	5,15	4,05 – 5,15 × 10 ¹² /L
Color index	0,9	0,85 – 1,15
Leukocytes	5,2	4,0 – 9,0 × 10 ⁹ /L
ESR	1	2-15mm/h
Stab neutrophils	2	1-6 %
Segmented neutrophils	58	47-72 %
Eosinophils	1	0,5-5,0%
Basophils	-	1-1,0 %
Lymphocytes	33	19-37%
Monocytes	6	3-11 %
Platelets	262,7	160-320 × 10 ⁹ /L

Conclusion: all parameters within the normal range

Urinalysis

Options	Results	NR
specific gravity	1,009	1,001-1,040
pH	6,0	5,0-7,0
protein	Not detected	to 0.033 g / l
glucose	Not detected	absent
leucocytes	1-2	6-8
epithelium	Not detected	≤15-20 squamous epithelial cells/hpf
bacteria	Not detected	absent

Conclusion: all parameters within the normal range

Biochemical panel

Options	Results	NR
Creatinine	88 $\mu\text{mol/l}$	44 – 124 $\mu\text{mol/l}$
eGFR	96 ml/min/1,73m^2	> 90 ml/min/1,73m^2
Urea	4,9 mmol/l	2,5 – 6,5 mmol/l
Uric acid	220 $\mu\text{mol/l}$	210 – 428 $\mu\text{mol/l}$
Glucose	5,4 mmol/l	4,1 – 5,5 mmol/l
Total protein	75 g/l	65 – 85 g/l

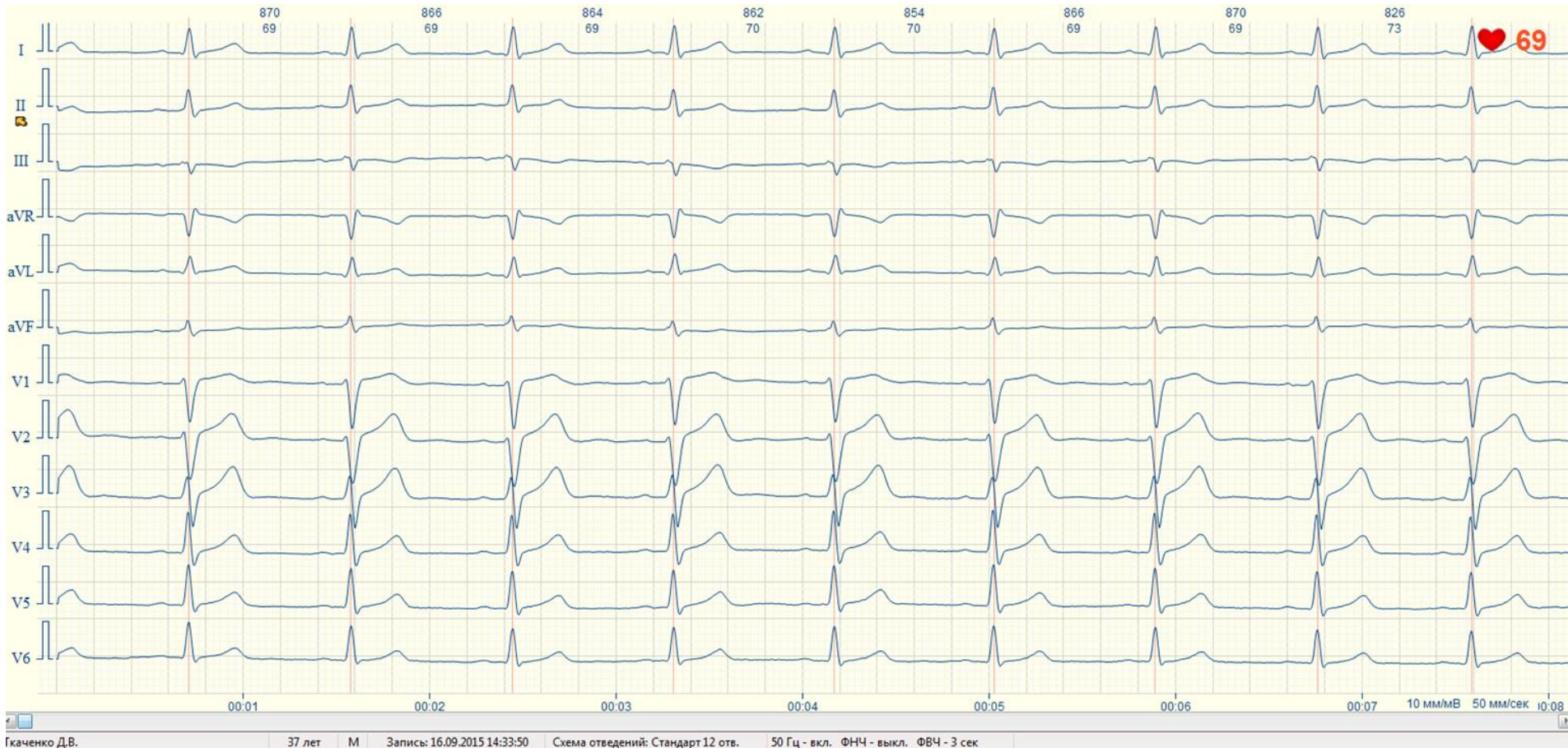
Conclusion: all parameters within the normal range

Lipid profile

Options	Results	NR
Total cholesterol	6,37 mmol/l	≤ 5,2 mmol / l
Very low-density lipoprotein cholesterol (VLDL-C)	0,37 mmol/l	up to 0,77 mmol/l
Low-density lipoprotein cholesterol (LDL-C)	4,47 mmol/l	up to 3,1 mmol/l
High-density lipoprotein cholesterol (HDL-C)	1,48 mmol/l	0,9 - 1,55 mmol / l
Triglycerides	0,83 mmol/l	<1,7 mmol/l
Atherogenic coefficient	3,27	Up to 3,0

Conclusion: dyslipidaemia with high levels of Total cholesterol, Low-density lipoprotein cholesterol and increased Atherogenic coefficient

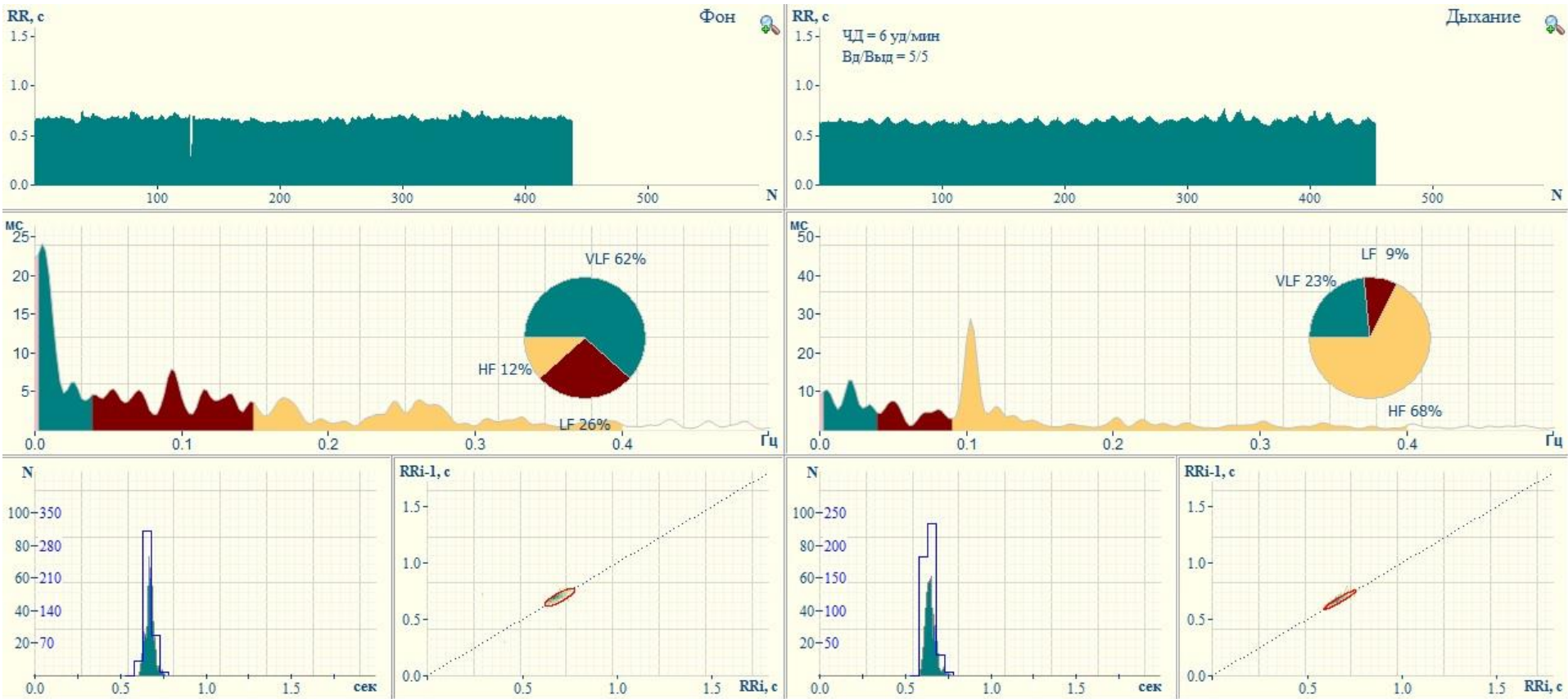
ECG



Conclusion: sinus rhythm with HR 70 bpm. Heart axis – horizontal position. Nonspecific ST-T changes in left ventricular posterior wall

Heart rate variability, breathing test

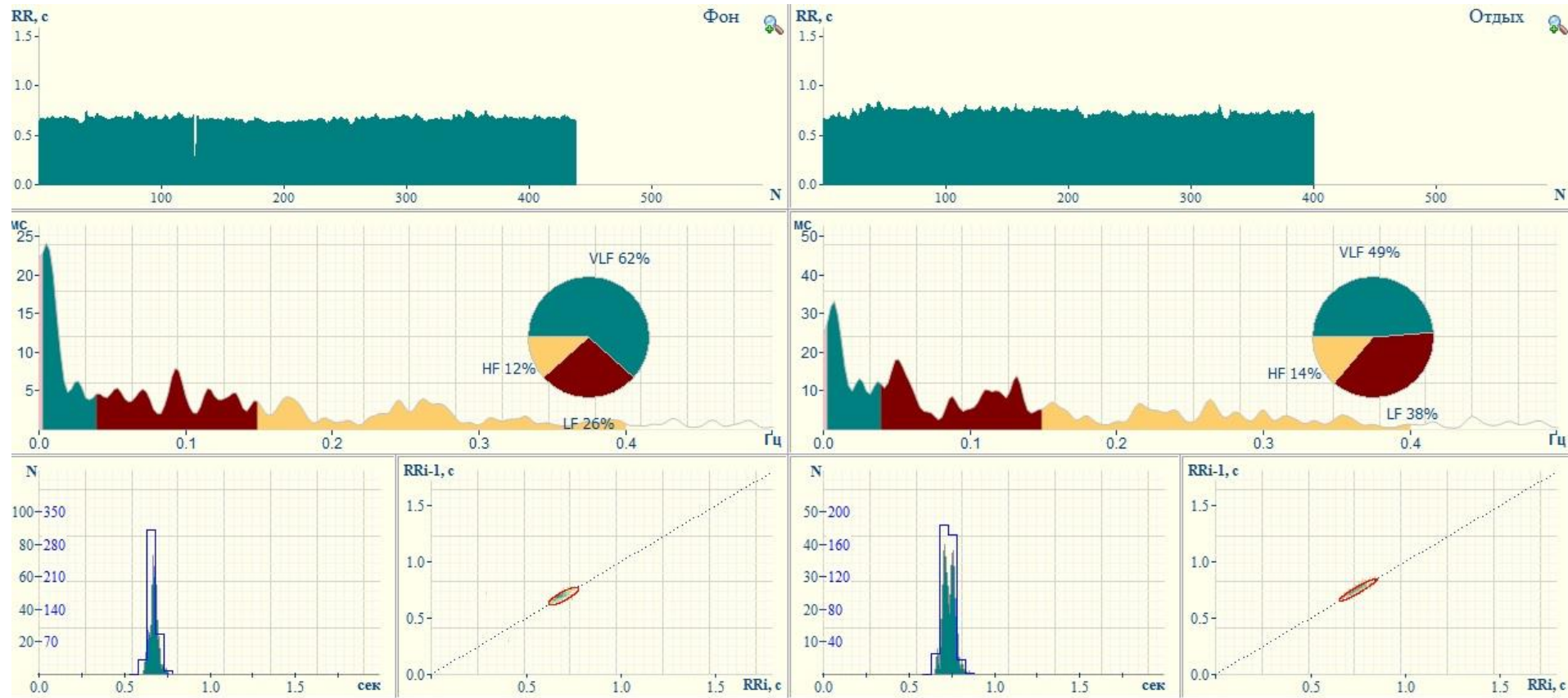
base level/breathing



The level of neurohumoral regulation (power spectral HRV) at rest is low, with the prevalence of humoral-metabolic regulation, which are not able to quickly provide homeostasis. Adequate reaction on breathing test.

Heart rate variability, breathing test

base level/rest



The nature of rhythm regulation at rest (after deep breathing) indicates a stabilization of heart rate with the transition of its regulation from the autonomic nervous system level to a lower humoral-metabolic level of regulation. Heart functionality is reduced.

EchoCG

Index	Data	NR
Posterior wall (diastole), cm	1.56	0.6–1.2
LV diastolic diameter, cm	5.2	4.3–5.9
IV septum (diastole), cm	1.55	0.6–1.3
LV mass, g	365.56	men < 183 g
LVM index, g/m ²	194.58	men < 115 g/m ² BSA
EF, %	60	55-60

LV – left ventricle, IV – intraventricular, LVM – left ventricle mass, BSA – body surface area, EF – ejection fraction

Conclusion:

- hypertrophy of the left ventricle
- satisfactory myocardial contractility

ABPM, daily means

SBP – systolic blood pressure, DBP – diastolic blood pressure, MAP – mean arterial pressure, PAP – pulse arterial pressure

Indices	Patient data	NR
SBP, daily mean, mmHg	142	No more than 130
DBP, daily mean, mmHg	85	No more than 80
MAP, daily mean, mmHg	103	80-95
PAP, daily mean, mmHg	57	Less than 46
SBP time index, %	79.1	Less than 15
DBP time index, %	64.8	Less than 15
SBP variability, mmHg	17.4	No more than 15
DBP variability, mmHg	19.9	No more than 14
MAP variability, mmHg	17.9	<i>no generally accepted normal values</i>
PAP variability, mmHg	14.7	<i>no generally accepted normal values</i>

stable mild systolic and borderline stable diastolic 24-h hypertension with increased SBP and DBP variability

ABPM, awake means

SBP – systolic blood pressure, DBP – diastolic blood pressure, MAP – mean arterial pressure, PAP – pulse arterial pressure

Indices	Patient data	NR
SBP, awake mean, mmHg	147	No more than 135
DBP, awake mean, mmHg	93	No more than 85
MAP, awake mean, mmHg	110	80-95
PAP, awake mean, mmHg	54	Less than 46
SBP time index, %	84,9	Less than 15
DBP time index, %	81,5	Less than 15
SBP variability, mmHg	16.6	No more than 15
DBP variability, mmHg	17.4	No more than 14
MAP variability, mmHg	14.9	<i>no generally accepted normal values</i>
PAP variability, mmHg	16.0	<i>no generally accepted normal values</i>

stable mild systolo-diastolic awake hypertension with increased SBP and DBP variability

ABPM, asleep means

SBP – systolic blood pressure, DBP – diastolic blood pressure, MAP – mean arterial pressure, PAP – pulse arterial pressure

Indices	Patient data	NR
SBP, asleep mean, mmHg	129	No more than 120
DBP, asleep mean, mmHg	65	50-70
MAP, asleep mean, mmHg	84	80-95
PAP, asleep mean, mmHg	64	Less than 46
SBP time index, %	67,7	Less than 15
DBP time index, %	31,9	Less than 15
SBP variability, mmHg	12,0	No more than 15
DBP variability, mmHg	9,6	No more than 14
MAP variability, mmHg	10,0	<i>no generally accepted normal values</i>
PAP variability, mmHg	7,4	<i>no generally accepted normal values</i>

stable mild systolic asleep hypertension with DBP mean and SBP/DBP variability within normal ranges

ABPM, daily BP profiles

Indices	Profile type	Night-time decline, %
SBP	Dipper	12,5
DBP	Overdipper	29,8
MAP	Overdipper	23,3
PAP	Nightpicker	- 18,5

SBP – systolic blood pressure, DBP – diastolic blood pressure, MAP – mean arterial pressure, PAP – pulse arterial pressure

- «dippers»** - physiological decrease in BP during the night - sleep-time relative BP decline 10-20% ;
- «overdippers»** - an excessive fall in BP at night, sleep-time relative BP decline > 20%;
- «nondippers»** - the lack of BP reduction at night, sleep-time relative BP decline < 10%;
- «night-peakers»** - night-time BP more than during daily activity, sleep-time relative BP decline < 0

Abdominal ultrasound

- The liver, gallbladder, pancreas, spleen, kidneys, thyroid gland - without changes, the pathology was not revealed

Abdominal CT scanning

The adrenal glands are located in a typical place, the right adrenal gland is not enlarged, legs up to 3 mm thick, with clear contours, homogeneous structure.

The left adrenal gland of normal size, with irregularly thickened legs from 3 to 8 mm, with clear contours, homogeneous structure. The surrounding fatty tissue is not changed.

Conclusion:

CT-signs of nodular hyperplasia of left adrenal gland.

The consultation of endocrinologist was recommended

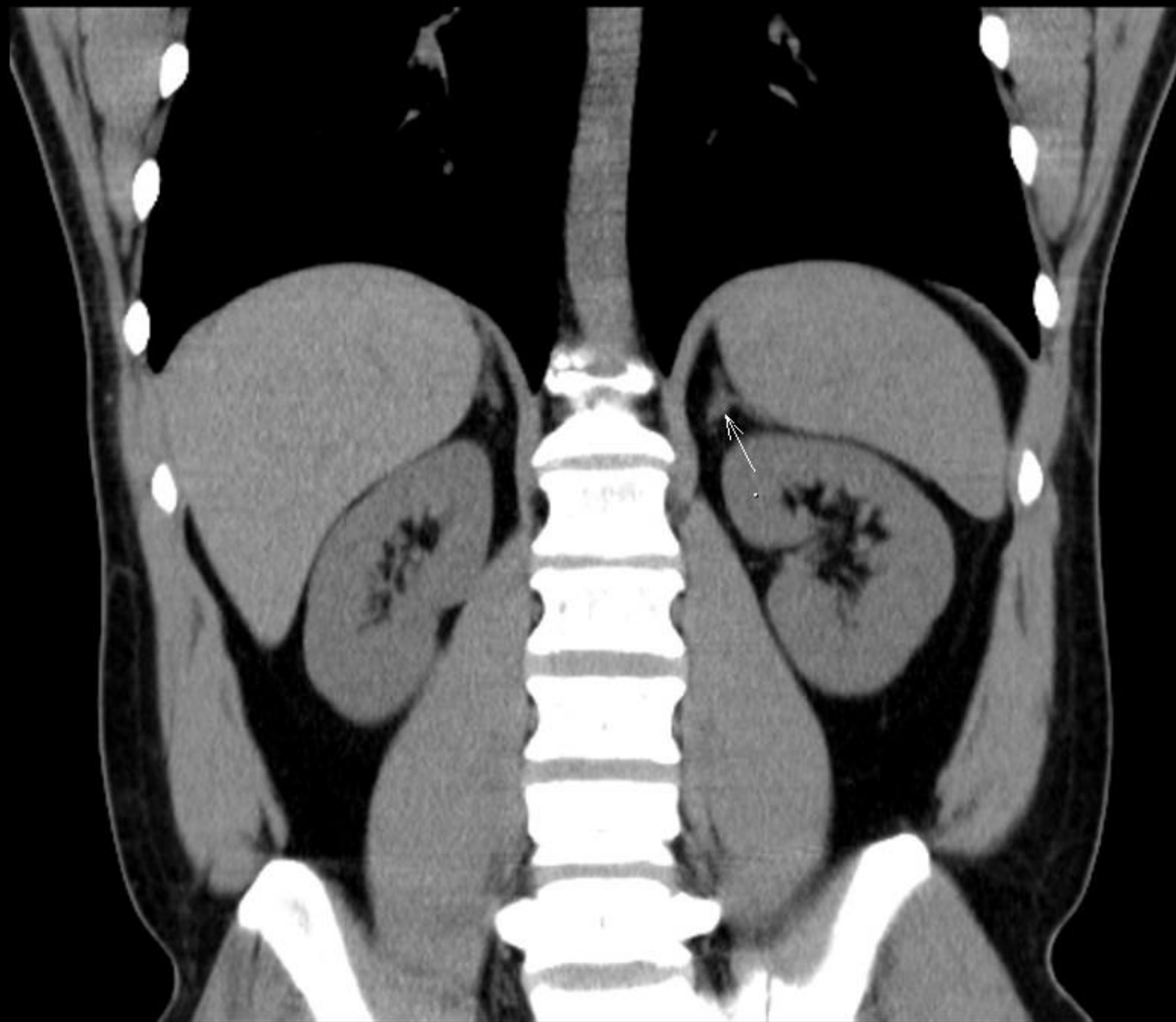
HRP

MDC LUX Kharkov
Emotion 16 (2010)



Spin: -90
Tilt: 24



Spin: 0
Tilt: -0

Consultation of endocrinologist

(with our comments)

- Conclusion: no data for pheochromocytoma
- *We still recommended to study the level of catecholamines and cortisol in blood, however, motivating with endocrinologist conclusion, the patient refused any further examination*

Risk factors	Diabetes mellitus	Asymptomatic organ damage
Male sex	FPG ≥ 7.0 mmol/L (126 mg/dL) on two repeated measurements, and/or	Pulse pressure (in the elderly) ≥ 60 mmHg
Age (men ≥ 55 years; women ≥ 65 years)	HbA1c $> 7\%$ (53 mmol/mol), and/or	Electrocardiographic LVH, or
Smoking	Post-load plasma glucose > 11.0 mmol/L (198 mg/dL)	Echocardiographic LVH [LVM index: men > 115 g/m ² (BSA)]
Dyslipidaemia	Established CV or renal disease	Carotid wall thickening (IMT > 0.9 mm) or plaque
Total cholesterol > 4.9 mmol/L (190 mg/dL), and/or	Cerebrovascular disease	Carotid–femoral PWV > 10 m/s
Low-density lipoprotein cholesterol > 3.0 mmol/L (115 mg/dL), and/or	CHD: MI; angina; myocardial revascularization with PCI or CABG	Ankle-brachial index < 0.9
High-density lipoprotein cholesterol: men < 1.0 mmol/L (40 mg/dL) and/or	Heart failure, including heart failure with preserved EF	CKD with eGFR 30–60 ml/min/1.73 m ² (BSA)
Triglycerides > 1.7 mmol/L (150 mg/dL)	Symptomatic lower extremities peripheral artery disease	Microalbuminuria
Fasting plasma glucose 5.6–6.9 mmol/L (102–125 mg/dL)	CKD with eGFR < 30 mL/min/1.73m ² (BSA); proteinuria (> 300 mg/24 h).	
Abnormal glucose tolerance test	Advanced retinopathy	
Obesity [BMI ≥ 30 kg/m ² (height ²)]		
Abdominal obesity (waist circumf.: men ≥ 102 cm in Caucasians)		
Family history of premature CVD (men aged < 55 years; women aged < 65 years)		

AH risk factors

Stratification of total CV risk for our patient

Other risk factors, asymptomatic organ damage or disease	Blood pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF		Low risk	Moderate risk	High risk
1–2 RF	Low risk	Moderate risk	Moderate to high risk	High risk
≥3 RF	Low to moderate risk	Moderate to high risk	High risk	High risk
OD, CKD stage 3 or diabetes	Moderate to high risk	High risk	High risk	High to very high risk
Symptomatic CVD, CKD stage ≥ 4 or diabetes with OD/RFs	Very high risk	Very high risk	Very high risk	Very high risk

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

Mancia G. 2013 ESH/ESC Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC) / Giuseppe Mancia, Robert Fagard, Krzysztof Narkiewicz[et al.] // Journal of Hypertension. – 2013. – Vol. 31, Is. 7. – P. 1281-1357.

Diagnosis

Arterial hypertension presumably of secondary origin (pheochromocytoma?), Grade 2, Stage II (LVH), high risk, with an excessive fall in DBP at night and physiological degree of sleep-time relative SBP decline, with adequate reaction on breathing test, HF 0. Nodular hyperplasia of left adrenal gland.

Treatment

- maintaining a healthy lifestyle
- decrease sodium intake
- lipid-lowering diet
- Diroton (lisinopril) 10 mg in the morning protractedly under the control of blood pressure level

Follow-up

- The patient was recommended to repeat the ABPM after 3 months, but at the appointed time the patient did not come. In a telephone conversation he said that he feels satisfactory, according to HBPM his BP is within 130-140/85 mm Hg, in further examination and observation he is not interested.
- It was recommended to continue Diroton intake, monitoring adrenal hyperplasia using abdominal CT-scanning yearly and measurements adrenal hormones in serum.

Questions?