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Surgical treatment in hypertension associated with adrenal diseases

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Abstract

Despite the recent advances in diagnosis and surgical treatment of hormonally active adrenal tumors (GAAT), the awareness of medical practitioners about the disease remains insufficient. The results of examination and treatment of 758 GAAT patients prove that long existing symptomatic (secondary) arterial hypertension (SHTN) is malignant characterized by the development of vascular complications involving cardiac and/or cerebral arteries, and drug-resistance and requires pre-surgery correction of metabolic and endocrine disorders. In GAAT, adrenalectomy is the main method of SHTN treatment. The reasons for maintaining or recurrence of arterial hypertension (HTN) after surgery in 35.7% of patients are not associated with surgery itself, but are due to the long duration of high blood pressure due to a 5.37 ± 3.30 years before the manifestation of the tumor in adult patients (older 44.75 ± 3.89 s), and co-existent endocrine, metabolic and cardiovascular disorders. The predominance of the pressor hormones over depressor ones leads to the cardiovascular remodeling, causes the development of left ventricular diastolic dysfunction due to impaired relaxation and the increased role of atrial systole in its filling. If these factors are identified, the selection and follow-up of the patients after surgery, and the choice of antihypertensive therapy are required. Early diagnosis of GAAT, adequate preoperative drug therapy, and implementation of timely surgical treatment contribute to the elimination of adrenal-related SHTN, provide good treatment results and better quality of life in GAAT patients.

Key words: symptomatic hypertension, hormonally active adrenal tumors, adrenalectomy

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Хирургическое лечение больных артериальной гипертензией надпочечникового генеза

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Резюме

Несмотря на то что за последние два десятилетия многие сложные вопросы диагностики и хирургического лечения больных гормонально-активными образованиями надпочечников (ГАОН) детально изучены, осведомленность практикующих врачей об этой патологии остается недостаточной. Анализ результатов обследования и лечения 758 больных ГАОН свидетельствует, что длительно существующая при этой патологии симптоматическая артериальная гипертензия (САГ) характеризуется злокачественным течением с развитием сосудистых осложнений в бассейне сердечных и/или мозговых артерий, трудно поддается антигипертензивной терапии и требует целенаправленной коррекции обменно-эндокринных нарушений перед хирургическим вмешательством. Установлено, что адреналэктомия у больных ГАОН является основным методом устранения САГ. Причины сохранения или рецидивирования артериальной гипертензии (АГ) у 35,7% оперированных не связаны с оперативным вмешательством, а обусловлены длительностью повышенного артериального давления более 5,37 ± 3,30 года до манифестации опухолевого процесса у пациентов зрелого возраста (старше 44,75 ± 3,89 года), эндокринно-обменными и сердечно-сосудистыми нарушениями. Преобладание прессорных гормонов над депрессорными приводит к ремоделированию сердечно-сосудистой системы, обусловливает развитие диастолической дисфункции левого желудочка вследствие нарушения релаксации миокарда и возрастания роли систолы предсердий в его наполнении. Выявление указанных факторов, способствующих сохранению или рецидиву АГ, требует подбора и проведения у прооперированных больных целенаправленной антигипертензивной терапии. Своевременная диагностика у больных ГАОН, проведение патогенетически обоснованной предоперационной медикаментозной подготовки и выполнение адекватного хирургического лечения способствуют устранению САГ надпочечникового генеза, обеспечивают хорошие результаты лечения и высокое качество жизни пациентов.

Ключевые слова: симптоматическая артериальная гипертензия, гормонально-активные опухоли надпочечников, адреналэктомия

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Arterial hypertension (HTN) is one of the most common chronic disease, affecting almost a quarter of the adult population and represents one of the main medical and social problems of the modern society on the prevalence and material loss caused to society [1–3].

Higher levels of blood pressure (BP) are associated with the direct increase in the risk of such diseases as atherosclerosis, ischemic heart disease (IHD), congestive heart failure (CHF) and acute cerebrovascular events (CVE) [4]. The monitoring Commission of the World Health Organization (who) established that the HTN-related complications lead to approximately 7.1 million deaths per year [3]. The main causes of symptomatic arterial hypertension (SHTN) include endocrine metabolic disorders which manifest in patients with adrenal tumors [5–10]. According to the epidemiological studies, they account for 5% to 13% of all HTN cases [3, 11].

Tumors of the cortex (aldosteronoma, corticosteroma) and medulla (pheochromocytoma) of the adrenal glands lead, respectively, to the overproduction of aldosterone, cortisol, adrenaline and noradrenaline. They are the most common endocrine causes of SHTN. Primary hyperaldosteronism (PHA), endogenous hypercortisolism, hypercatecholaminemia are the common clinical syndromes which primarily manifest as resistant hypertension and its complications [12–16].

When associated by HTN, the diagnosis of adrenal disease is not difficult; however, interpretation might be still complicated. This is due to the gradual development of clinical symptoms as a result of the overproduction of adrenal hormones, which lead to the BP elevation as the only manifestation. Furthermore, due to the lack of the medical vigilance and the ignorance of clinical symptoms these patients are considered to suffer from hypertensive disease (HD). However, ongoing antihypertensive therapy commonly is not efficient. Therefore, timely diagnostics of adrenal tumors and surgical treatment, in the majority of cases, contribute to the normalization of BP and/or a more favorable outcomes of HTN [17–23].

The purpose of the study was to evaluate the effectiveness of the diagnostic procedures, the perioperative treatment and the results of operative interventions in patients with adrenal disease-related HTN.

Design and methods

In the clinic of surgery n. a. S. P. Fedorov of the Military Medical Academy n. a. S. M. Kirov, 1035 patients with surgical diseases of the adrenal glands were diagnosed and treated. Depending on the nosology, the ratio was the following: 758 patients had hormonally active adrenal tumors (HAAT), 283 (37.4%) patients were operated for aldosteronoma, 228 (30.1%) received corticosterone, chromaffinoma was diagnosed in 247 (32.5%) patients.

The average age of patients at the time of the examination and treatment ranged from 15 to 79 years (mean age 41.09 ± 3.10 years, in women — 40.75 ± 2.90 years, in men — 41.47 ± 3.1 years).

All patients underwent a comprehensive examination, including clinical, biochemical, hormonal, radiological methods, according to the common clinical algorithm [18, 20, 21, 24].

We studied the hormones in the blood plasma (ACTH, cortisol, metanephrine, normetanephrine, plasma renin activity), including the precursors of corticosteroids using the method of high performance liquid chromatography (HPLC) [25, 26,12].

To verify the clinical forms of PGA we conducted functional studies (marching and verospiron tests) to identify the autonomous secretion of aldosterone [5,27].

Specialized instrumental methods included ultrasonography (USG) (including intraoperative procedure), computed tomography (CT), magnetic resonance imaging (MRI), angiography, selective venography with separate blood sampling from the adrenal glands [9, 28, 29].

Cardiovascular parameters and central hemodynamics before surgery were studied using the daily BP monitoring, Holter ECG monitoring, echocardiography, integral body rheography (IBRH), respiratory function (ERF), intraoperative monitoring of the cardiovascular and respiratory systems [30]. These ivestigations allowed to evaluate the functional reserves beore surgery and to perform preventive procedures [18, 20, 24].

This approach in the assessment of the cardiovascular and respiratory systems in HAAT patients

provided reliable prevention of complications at all stages of the perioperative period.

Morphological examination of the removed adrenal gland with the tumor was the final stage of diagnostics. Histological examination of deleted saples was guided by the current International histological classification of endocrine tumors [31]. We studied the histology of both the tumor tissue and changes in the structure of the adrenal gland outside the tumors. Histological and electron-microscopic studies were performed according to standard techniques published elsewhere [32].

Results and discussion

HTN of varying severity before the operation was diagnosed in 678 (89.4%) patients with hormonally active tumors of the adrenal glands. In 36.4% of patients it led to the development of severe hemodynamic disturbances and complications (Table 1).

Primary hyperaldosteronism due to aldosterone secreted aldosteronoma (ASA) of the adrenal cortex was diagnosed in 283 patients. Our studies showed that significant ($p < 0.05$) ASA signs (sensitivity 97.5%) are: low-renin HTN with blood level of aldosteron of more than 500 PG/ml, positive marching test and the presence of a rounded tumor in one adrenal gland with a diameter from 0.6 to 4.0 cm (2.46 ± 1.41 cm) with a density of 11.5 ± 3.4 HU, which increased to 30.0 ± 2.8 HU after intravenous contrast enhancement during CT scanning [20, 21].

Typical clinical manifestations of ASA, characterized by the presence of HTN, dysuric disorders and neuromuscular syndrome were observed in 49.4% of patients. Atypical variant implying the presence of one or two syndromes is diagnosed in 50.6% of the patients (including 6.6% asymptomatic patients and those with rare episodes of moderate blood pressure elevation). Therefore, our results do not confirm that only typical clinical manifestation of ASA is PHA [13].

The average duration of HTN in patients with ASA was up to 7.02 ± 3.15 years and was characterized by hypertensive crisis in more than 60.3% cases. Long-existing HTN in 20.6% of PHA patients led to the development 1–3 vascular complications by the time of diagnosis (Table 1).

We were especially interested in the atypical ASA manifestations found in 6.6% patients (subclinical form) with no clinical manifestations of PHA or rare episodes of moderate blood pressure in-

Table 1

COMPLICATIONS OF ARTERIAL HYPERTENSION IN PATIENTS WITH HORMONALLY ACTIVE ADRENAL TUMORS

Complications	The number of patients (%)		
	Aldosteronoma	Corticosteroma	Chromaffinoma
Heart failure class II (NYHA)	–	16.4	22.6
Heart failure class III (NYHA)	–	9.3	51.7
Heart failure class IV (NYHA)	–	–	14.6
Acute cerebrovascular event	9.8	7.1	10.2
Acute myocardial infarction	0.8	3.2	5.1
Acute heart failure with pulmonary edema	–	2.8	1.5
Angioretinopathy	3.3	6.7	11.7
Catecholamine myocardiodystrophy	–	–	8.0
Epistaxis	–	–	2.9
Nephropathy	5.1	25.9	5.1
Type 2 diabetes mellitus or impaired glucose tolerance	–	29.6	5.1
Encephalopathy	1.6	8.2	1.5

crease. Regrading hormonal status, the plasma aldosterone was normal or at its upper reference limit, the plasma renin activity was within normal range or at its lower limit. However, detailed investigation of the endocrine profile by HPLC showed statistically significant ($p < 0.05$) increase in the secretion of hormones precursors of corticosteroids (11-desoxycortisol to 7.46 ± of 4.02 (normal: 1–3 ng/ml) and 11-deoxycorticosterone to 7.3 ± 4,8 (normal: < 2 ng/ml), indicating the initial stages of ASA. The corticosterone was not significantly elevated ($p > 0.05$) [21].

The clinical manifestations of the endogenous hypercortisolism syndrome in 228 (of 30.1%) patients are characterzed by multiplicity and specificity. Changes in the appearance of these patients were the first symptoms to call attention of the out-patient doctors. By the severity of clinical symptoms, patients are divided into two groups. The first group (71.1%) consisted of patients with typical clinical manifestations. Beside the specific changes in appearance, all these patients had HTN, among them 22.2% of patients showed hypertensive crises with the increased of systolic blood pressure up to 200–220 mmHg. Heart rhythm disturbances occurred in 28.9% patients. At the same time, no relation was found between the HTN degree and the duration of the disease. The vast majority of patients (94.7%) demonstrated myocardial changes (according to ECG), signs of heart failure were found in 44.4%.

The second group (28.9%) included patients with subclinical signs of endogenous hypercortisolism. All of them lacked specific manifestations of the disease.

The level of adrenocorticotropic hormone (ACTH) was normal and amounted to 2.5 ± 1.1 pmol/l ($p < 0.001$), while the concentration of cortisol in blood plasma was increased up to 987 ± 248 nmol/l ($p < 0.001$). Free cortisol and daily 17-OKS urine excretion were also increased — 46.2 ± 12.4 μmol/l/s and 645 ± 174.3 nmol/l ($p < 0.001$), respectively. A large dexametasone test showed that on the 3rd day these parameters decreased by less than 50%, which confirms the autonomous overproduction of corticosteroids by the adrenal tumor ($p < 0.001$). The patients with subclinical endogenous hypercorticism with the moderate increase of plasma cortisol are characterized by statistically significant ($p < 0.05$) increase in the corticosteroids precursors: 11-desoxycortisol to 11.3 ± 3.1 (normal level: 1–3 ng/ml), 11-deoxycorticosterone to 12.3 ± 2.3 (normal level: < 2 ng/ml), of corticosterone to 9.1 ± 2.3 (normal level: < 3 ng/ml).

CT scans identified corticosteron-secreting tumors as a rounded neoplasm with clear and smooth contours, diameter of 20–30 mm, and native density of 19.3 ± 2.2 HU with uniform contrast accumulation of the drug in the parenchymal phase scan to 46.0 ± 3.4 HU at delayed scan up to 18.0 ± 3.4 HU [32].

Based on the examination of 247 (32.5%) patients with chromaffinoma, hypertension was diagnosed in 90.1% patients. Three groups were formed based on BP characteristics: 1) paroxysmal form of HTN was diagnosed in 53.3%; 2) mixed HTN — 36.8%; 3) normal blood pressure — 9.9%.

In paroxysmal form, hypertensive crises are characterized by the blood pressure elevation up to 260/140–300/180 mm Hg and above. BP remains normal between crises. The attacks are accompanied by the neuro-vegetative manifestations: headache (90.1%), palpitations (83.9%) and sweating (79.0%), blanching (19.7%) or redness (59.2%) of the skin, fear of the death, paresthesia (24.7%), impaired vision (41.9%) [24].

Mixed form of HTN is observed in 36.8% of patients with chromaffinoma. It is characterized by constantly high BP up to 150–200/100–120 mmHg and hypertensive crises. During the crisis BP increases up to 240–260/150–170 mmHg. The average systolic blood pressure (out of crisis) is 178.0 ± 8.4 and 108.0 ± 7.6 mmHg. Catecholamine crises are less typical than in patients with the paroxysmal form. Mixed form of HTN appeared to be more difficult to be diagnosed due to the not clear neuro-vegetative manifestations.

Moreover, headache and heart pain, weakness, palpitations, swelling of the lower extremities in patients with mixed HTN can be also seen in essential HTN, especially in elderly patients. Clinically chromaffinoma could masquerade as IHD with acute or chronic heart failure. Often, the complete regression of the ECG signs of extensive ischemia or myocardial "pseudoinfarction" led to the more detailed search of a tumor.

Clinical manifestations of pheochromocytoma extensively vary, causing significant difficulties in making timely diagnosis. Due to the clinical variability, 82.5% patients with high blood pressure had been treated for essential HTN, IHD, neurocirculatory dystonia for a long time (2 to 30 years).

The average disease duration in patients with mixed HTN was longer (6.94 ± 2.66) than in patients with the paroxysmal form, however, these differences were not significant ($p > 0.05$). In addition, 26% patients with mixed form of HTN were aged 58.27 ± 2.47 years, and paroxysms were preceded by "essential" HTN on average for 18.27 ± 3.15 years ($p < 0.05$). Therefore, the diagnostics of chromaffin tumors is difficult in elderly patients, suffering from long-lasting IHD with heart failure development [19].

However, long-existing HTN with undiagnosed pheochromocytoma demonstrates a lack of awareness among the clinicians. Due to the low awareness, laboratory and instrumental diagnostics are delayed at the prehospital stage and was performed for the failure of antihypertensive therapy, as well as for the the development of severe complications (Table 1).

Chromaffinoma was diagnosed based on increased urinary catecholamine excretion in patients with paroxysmal or mixed HTN, which showed sensitivity 78% and specificity 82.1%. In case of normal urine catecholamine excretion in patients with clear manifestations of the tumor or masked/absent HTN, blood level of metanephrine and normetanephrine are examined, showing sensitivity and specificity of 100% and 95.8%, respectively.

Table 2

CENTRAL HEMODYNAMICS AND RESPIRATORY FUNCTION IN PATIENTS WITH HORMONALLY ACTIVE ADRENAL TUMORS IN PREOPERATIVE PERIOD (M ± m)

Parameters	In healthy people	Aldosteronoma		Corticosteroma		Chromaffinoma	
		baseline	2 weeks later	Baseline	2 weeks later	baseline	2 weeks later
Stroke volume index, ml/m^2	44,5 ± 6,0	29,2 ± 1,2	34,9 ± 2,1*	28,4 ± 1,4	35,5 ± 3,7*	32,6 ± 3,3	36,7 ± 2,4*
Cardiac index, l/min/m^2	3,1 ± 0,7	2,2 ± 0,4	2,9 ± 0,4*	2,4 ± 0,2	2,8 ± 0,1*	2,3 ± 0,1	2,9 ± 0,2*
Reserve ratio, c.u.	1,0 ± 0,1	0,76 ± 0,2	0,87 ± 0,1*	0,71 ± 0,1	0,95 ± 0,1*	0,78 ± 0,1	0,96 ± 0,1*
Coefficient of respiratory changes, c.u.	1,16 ± 1,24	1,32 ± 0,1	1,16 ± 0, 1*	1,2 ± 0,2	1,16 ± 0,1*	1,6 ± 0,2	1,17 ± 0,2*
Indicator of the breath tension, c.u.	не > 26,5	28,1 ± 1,9	21,2 ± 3,7*	27,3 ± 1,1	23,1 ± 2,3*	28,34 ± 5,4	22,5 ± 2,1*
Index of the tissues hemodynamic security, c.u.	1,0 ± 0,2	0,78 ± 0,1	1,0 ± 0,1*	0,7 ± 0,1	1,1 ± 0,2*	0,77 ± 0,13	0,9 ± 0,1*

Note: M — arithmetic mean value; m – confidence interval; p – test of significance; * – statistically significant index variation, $p < 0.05$.

Among modern radiology studies, ultrasound and CT (when combined the sensitivity increases up to 97.8 %) are compulsory diagnostic procedures, comparable with MRI. CT demonstrates 100 % specificity in identifying chromaffinoma when the density of the tumor is 38.78 ± 3.46 units Hu and it increases to 50.62 ± 2.50 units Hu when contrast agents.

A comprehensive cardiovascular assessment in patients with HAAT showed that most of them had a decrease of cardiac output and the resting minute blood volume [19, 21]. Moreover, at standard physical activity no incresase was observed, unlike healthy people. Heart failure and reduced reserve myocardial capacity were confirmed in all patients at admission to the clinic (Table 2).

High systemic vascular tone in almost all patients reflected peripheral vasoconstriction, reduced circulation capacity and circulation centralization.

Preoperative preparation was very important. Drug therapy included antihypertensive medications, correction of hypokalemia, hypernatremia and metabolic alkalosis. The treatment included aldosterone receptor antagonists (spironolactone), angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers. After 1.5–2 weeks the combination therapy led to the BP reduction or normalization, elimination of extensive fluid and electrolyte and hormone imbalances, which is consistent with the other studies [1, 8, 20].

The main objective of preoperative preparation in patients with corticosteroma was to obtain normal plasma levels of cortisol. For this purpose, we used orimeten with a gradual dosage increase: 1st week — 250 mg/day; 2nd week — 500 mg/day; 3rd week — 750 mg/day. With the maximum dosage the cortisol plasma levels were normalized, systolic BP reduced and the main hemodynamic parameters improved, according to the IRHB [18].

Preoperative medical support was carried out in all patients with chromaffinoma and did not differ from the schemes published elsewhere [1, 4, 19]. Alpha-blockers (phenoxybenzamine, prazosin, agents, pirroksan) were essential and were prescribed to 98 % patients. Also beta-blockers (atenolol, metoprolol, propranolol) were prescribed to 68 % and angiotensin-converting enzyme inhibitors (captopril, enalapril) or calcium channel blockers (diltiazem, nifedipine) — to 34 %. In patients with chromaffinoma cardiac output is maintained by tachycardia due to low stroke volume, so early prescription of β-blockers (before α-blockers), which reduce heart rate, can provoke heart failure. Normotensive patients without hypertensive crises and normal plasma and urine catecholamine levels do not require specific preoperative preparation.

We found heart failure signs in 88.9 % patients with chromaffinoma. Among them 66.4 % patients had IV anaesthetic-related risk (ASA classification), so the planned surgery was contraindicated. Preoperative preparation was implied to prevent cardiopulmonary decompensation by increasing reserve myocardial capacity, correction of metabolic and hormonal disorders. As a result, all patients with chronic heart failure after the preoperative preparation leading to the reduction in anaesthetic-related risk (to III ASA score) were operated [24].

Assessment of the cardiovascular and respiratory reserve in HAAT patients showed an adequate response to the standard physical activity after 2-week preoperative preparation (Table 2). Minute blood circulation volume increased and was 24 % more than before the training. Both heart rate and cardiac output (approximately in equal proportion) increased.

Surgical intervention nowadays is considered the main approach to treat adrenal-related hypertension. In the majority of cases it allows to achieve clinical recovery in the short-term and late postoperative period [1, 19, 21, 23, 34].

All patients underwent surgery in the clinic and endovideosurgical methods.were applied in the majority of cases (92 %). Laparoscopic and retroperitoneoscopic adrenalectomy allowed us to determine personalized optimal approach for each patient which helped to minimize intra- and postoperative complications and to avoid lethal cases. After endovideosurgical adrenalectomy all patients reported mild pain, which stoped after non-opioid analgesics. Early mobilization was applied in the first days after the operation in all patients. Rapid recovery of the gastrointestinal motility on the second day, social and labor rehabilitation, and the high quality of life at long–term follow-up were observed in all patients [19, 21].

At the remote follow-up, persistent BP normalization was achieved in 64.3% patients with HAAT, 35.7% demonstrated hypertension, which was preserved immediately after surgery or recurred subsequently (within 4.3 ± 3.4 years). In all cases, the course of HTN was much more favourbale than before the operation, and BP was well-controlled by conventional drugs (bisoprolol, fosinopril, enalapril, metoprolol, etc.). Targeted clinical, laboratory and instrumental examination showed no signs of adrenal tumor recurrence. The persistence or recurrence of HTN was observed in patients who were in adulthood at the time of surgical intervention. Persistent postoperative HTN (20%) was found in the elderly patients (aged 58.80 ± 2.07 years) compared to younger patients with transient HTN (15.7%) (aged 44.75 ± 3.89 years). The mean age of normotensive patients in postoperative period, at the time of tumor removal was 34.75 ± 3.27 years. Therefore, the groups differed significantly by age at the time of surgery ($p < 0.05$), which might explain the reasons for the persistence or recurrence of HTN in the remote postoperative period. Our findings suggest that hormone-active tumors developed in patients aged 44.75 ± 3.89 years, who commonly had essential HTN. In addition, persistent HTN had preceded tumor manifestation for 13.60 ± 3.27 years ($p < 0.05$) and emerged after the operation. On the other hand, in patients with transient and permanent HTN and BP normalization after surgery, hypertension history amounted up to 5.37±3.30 years. Therefore, we suggest that the reasons for HTN persistence or occurrence after tumor removal are not associated with inadequate surgical intervention or recurrence of the disease [19, 21].

The long-existing hyperproduction of cortical or medullar hormones is an important factor in maintaining HTN after HAAT removal and leads to btoh pro-hypertensive endocrine (activity of renin, aldosterone, deoxycorticosterone), and depressor inhibition — decreased secretion of prostaglandin E2. These changes significantly affect the BP increase during physical exertion and in stressful situations. The predominance of pressor hormones over the depressor seem to result in cardiovascular remodeling. Ultimately, this contributed to the development of left ventricular diastolic disfunction due to impaired myocardial relaxation and the increasing role of the atrial systolic filling, which is consistent with other authors [2, 30, 35, 36].

Thus, the symptomatic adrenal disease-related HTN is an interdisciplinary issue, since HTN is considered a significant factor of coronary heart disease, kidney failure, stroke, heart failure and, consequently, a cause of disability and mortality. Close collaboration between surgeons, physicians and endocrinologists allows to obtain satisfactory results in all HAAT patients in case of timely diagnosis and adequate intervention.

Conflict of interest

The authors declare no conflict of interest.

Список литературы / References

1. Kalinin AP, Maystrenko NA, Vetshev PS. Surgery in endocrinology. Ed. by AP Kalinin, NA Maystrenko, PS Vetshev. St Petersburg: Piter, 2004. 941 p. In Russian.

2. Mancia G, Fagard R, Narkiewicz K, Redón J, Zanchetti A, Böhm M et al. 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). J Hypertens. 2013;31(7):1281–1357. doi:10.1097/01.hjh.0000431740.32696.cc

3. Redon J, Olsen MH, Cooper RS, Zurriaga O, Martinez-Beneito MA, Laurent S et al. Stroke mortality trends from 1990 to 2006 in 39 countries from Europe and Central Asia: implications for control of high blood pressure. Eur Heart J. 2011;32(11):1424–1431. doi:10.1093/eurheartj/ehr045

4. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988–2008. J Am Med Assoc.2010;303(20):2043–2050. doi:10.1001/jama.2010.650

5. Vetshev PS, Polunin GV. Disputable and unsolved questions in diagnostics and operative treatment in primary hyperaldosteronism (to the 50-year anniversary of the first description of Conn's syndrome).Surgery. 2006;1:17–21. In Russian.

6. Birns J, Kalra L. Cognitive function and hypertension. J Hum Hypertens. 2009;23(2):86–96. doi:10.1038/jhh.2008.80

7. Diez J. Effects of aldosterone on the heart: Beyond systemic hemodynamics? Hypertension. 2008;52(3):462–464. doi:101161/HYPERTENSIONAHA/108/117044

8. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. Br Med J. 2009;338: b1665.doi:10.1136/bmj.b1665

9. Mulatero P, Stowasser M, Loh KC, Fardella CE, Gordon RD, Mosso Let al. Increased diagnosis of primary aldosteronism, including surgically correctable forms, in center five continents. J Clinic Endocrinol Metab. 2004;89(3):1045–1050. doi:10.1210/jc.2003–031337

10. Rossi GP, Bernini G, Caliumi C, Desideri G, Fabris B, Ferri C et al. A prospective study of the prevalence of primary aldosteronismin 1,125 hypertensive patients. J Am Coll Cardiol. 2006;48(11):2293–3000. doi:10.1016/j.jacc.2006.07.059

11. Pereira M, Lunet N, Azevedo A, Barros H. Differences in prevalence, awareness, treatment and control of hypertension between developing and developed countries. J Hypertens. 2009;27 (5):963–975.

12. Eisenhofer G, Kopin IJ, Goldstein DS. Catecholamine metabolism: a contemporary view with implications for physiology and medicine. Pharmacol Rev. 2004;56 (3):331–349. doi:10.1124/pr.56.3.1

13. Hannemann A, Wallaschofski H. Prevalence of primary aldosteronism in patient's cohorts and in population-based studies: a review of the current literature. Horm Metab Res. 2012;44(3):157–162.

14. Hickman PE, Leong M, Chang J, Wilson SR, McWhinney B. Plasma free metanephrines are superior to urine and plasma catecholamine metabolites for the investigation of pheochromocytoma. Pathology. 2009;41(2):173–177. doi:10.1080/00313020802579284

15. Grouzmann E, Drouard-Troalen L, Baudin E, Plouin PF, Muller B, Grand Det al. Diagnostic accuracy of free and total metanephrines in plasma and fractionated metanephrines in urine of patients with pheochromocytoma. Eur J Endocrinol. 2010;162(5):951–960. doi:10.1530/EJE-09–0996

16. Peaston RT, Graham KS, Chambers E, van der Molen JC, Ball S et al. Performance of plasma free metanephrines measured by liquid chromatography-tandem mass spectrometry in the diagnosis of pheochromocytoma. Clin Chim Acta. 2010;411(7–8):546–552. doi:10.1016/j.cca.2010.01.012

17. Shustov SB, Yakovlev VA, Baranov VL, Karlov VA. Arterial hypertension. Ed. by SB Shustov. St Petersburg: Special'naya literatura, 1997. 320 p. In Russian.

18. Dovganyuk VS. Modern operative approaches in adrenal tumors: Doctoral Thesis. St Petersburg, 2005. 280 p. In Russian.

19. Майстренко Н. А. Хромаффинные опухоли. СПб.: Наука, 2007. 250 с. [Maystrenko NA. Chromaffin Tumors. St Petersburg: Nauka, 2007. 250 p. In Russian].

20. Lysanyuk MV. Differential diagnostics and management approach in primary hyperaldosteronism: PhD Thesis. St Petersburg, 2010. 164 p. In Russian.

21. Romaschenko PN, Maystrenko NA. Hyperaldosteronism. St Petersburg: Piter, 2011. 251 p. In Russian.

22. Schwartz AE, Pertsemlidi D, Gagner M. Endocrine surgery. New York: Basel Dekker, 2004. XVIII. 712 p.

23. Pacak K, Eisenhofer G, Ahlman H, Bornstein SR, Gimenez-Roqueplo AP, Grossman AB et al. Pheochromocytoma: recommendations for clinical practice from the First International Symposium. Nat Clin Pract Endocrinol Metab. 2007;3(2):92–102. doi:10.1038/ncpendmet0396

24. Romashchenko PN. Modern approaches to the diagnostics and operative managements of chromaffin tumors: Doctoral Thesis. St Petersburg, 2007. 342 p. In Russian.

25. Velikanova LI. Information value of laboratory technologies for the development of diagnostic algorithms in adrenal tumors: Doctoral Thesis. Moscow, 2005. 40 p. In Russian.

26. Ito Y, Obara T, Okamoto T, Kanbe M, Tanaka R, Iihara M et al. Efficacy of single-voided urine metanephrine and normetanephrine assay for diagnosing pheochromocytoma. World J Surg. 1998;22(7):684–688.

27. Garagezova AR. Diagnostics and operative treatment in primary aldosteronism: Doctoral Thesis. Moscow, 2002. 44 p. In Russian.

28. Kurianov DP. Optimization of radiology diagnostics approaches in adrenal pathology: PhD Thesis. Kazan, 2009. 93 p. In Russian.

29. Young WF, Stanson AW, Thompson GB, Grant CS, Farley DR, van Heerden JA. Role for adrenal venous sampling in primary aldosteronism. Surgery. 2004;136(6):1227–1235. doi:10.1016/j.surg.2004.06.051

30. Barsukov AV, Shustov SB. Arterial hypertension: clinical phenotyping and therapy choice. St Peters-burg: ELBI-SPb, 2004. 249 p. In Russian.

31. Solcia E, Kloppel G, Sobin LH. Histological typing of endocrine tumors. WHO Classification of Endocrine Tumours. Berlin: Springer-Verlag, 2000. 160 p. doi:10.1007/978–3-642–59655–1

32. Kazantseva IA, Kalinin AP, Polyakova GA. Clinical morphology of cortical tumors and adrenal hyperplasia (textbook). Moscow: MONIKI, 1998. 35 p. In Russian.

33. Maystrenko NA, Zheleznyak IS, Romashchenko PN, Blyumina SG. Computer scan sinadrenal surgery. Vestnik Khi-rurgii = Bulletin of Surgery. 2015;174(6):23. In Russian.

34. Shevchenko Yu L, Vetshev PS, Podzolkov VI, Ippolitov LI, Rodionov AV, Polunin GV. Novel aspects of diagnostics and management of adrenal-related symptomatic hypertension. Therapeutic Archive. 2003;75(4):8–15. In Russian.

35. Nechesova TA, Korobko IYu, Kuznetsova NI. Left ventricular remodeling: pathogenesis and evaluation techniques. Meditsinskiye Novosti = Medical News. 2008;11:7–13. In Russian.

36. Rossi GP, Bolognesi M, Rizzoni D, Seccia TM, Piva A, Porteri E et al. Vascular remodeling and duration of hypertension predict outcome of adrenalectomy in primary aldosteronism patients. Hypertension. 2008;51(5):1366–1371. doi:10.1161/HYPERTENSIONAHA.108.111369

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