

# PRIMARY ALDOSTERONISM: THE RESULTS OF THE TREATMENT ACCORDING TO THE DATA OF RENAL ARTERIES DUPLEX SCANNING

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## ABSTRACT

In the structure of arterial hypertension, primary aldosteronism (PA) ranges from 5 to 15%. Changes in intrarenal hemodynamics are due to both high blood pressure and direct aldosterone level. The purpose of the study was to analyze the results of PA treatment according to ultrasound doppler scanning of renal arteries. In general, 55 patients with PA were treated. Renal arteries duplex scanning before and after the treatment was performed in 20 patients. During treatment, the normalization of Vps, Ved, S/D, PI, AT, TAMX indices was recorded in patients. The RI of the interlobar arteries slightly increased, however, it remained within the reference range. The reduction of aldosterone levels led to increase of TAMX index at the level of the renal artery trunk, S/D, RI and decrease in AT at the level of the segmental arteries, as well as increase of Ved and S/D at the level of the interlobar arteries.

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Endocrine pathology of the adrenal glands causes the development of arterial hypertension. In the structure of arterial hypertension primary aldosteronism ranges from 5 to 15%. A slightly higher part of this pathology in the structure of resistant arterial hypertension is 20% [1, 2, 3].

The question of the effect of aldosterone on intrarenal hemodynamics in patients with primary aldosteronism is important. Changes in the state of intrarenal hemodynamics are due not only to the effect of arterial pressure in this category of patients, but also directly to aldosterone [4, 5, 6].

In patients with excessive aldosterone, organic and functional changes in the vascular bed are more obvious compared with patients with essential hypertension. The greater vulnerability to fibrous changes in small diameter vessels is important [7, 8]. A number of performed histological studies of the structure of the vascular walls showed that in patients with primary aldosteronism there is an increase in total collagen and vascular collagen of the 3rd type, which is treated by an increase in the ratio of thickness of the medial vascular tunic to intima [9, 10]. The question of the study of the features of hemodynamics of intrarenal hemodynamics before and after hospital stages is interesting.

**Purpose of the study.** To analyze the results of primary aldosteronism treatment according to ultrasound doppler scanning of renal arteries.

**Materials and methods.** For the period from 2014 to February 2019, 145 patients with adrenal pathology were examined and treated in the hospital of the ZSMU Hospital on the basis of the Transplantation and Endocrine Surgery Department of the Public Institution "Zaporizhzhya Regional Hospital" of Zaporizhzhya Regional Council.

Primary aldosteronism is diagnosed in 55 patients. The renal hemodynamics by means of ultrasound doppler scanning before and after treatment were investigated in 20 (36.4%) patients: 12 (60%) women and 8 (40%) men. The average age of the patients is  $50.7 \pm 13.9$  years.

Diagnosis was performed according to clinical practical guidelines for the diagnosis and treatment of primary aldosteronism (Clinical Practical Guideline - Management of Primary Aldosteronism; 2016) [11].

According to the computer tomography, the structure of adrenal pathology was as follows: right side pathology had 1 patient (5%), left side - 10 patients (50%), bilateral - 9 (45%) ones. Taking into account the cations, the patients received treatment for primary aldosteronism: 3 (15%) patients had X-ray endovascular destruction of adrenal glands, 9 (45%) patients had laparoscopic adrenalectomy, and conservative therapy was prescribed to 8 (40%) patients.

Ultrasound doppler scanning of renal arteries was performed on an ultrasound diagnostic doppler apparatus called PhilipsEnVisor HD using a 3.5 MHz curvilinear transducer (Philips, the Netherlands). The study was performed on an empty stomach in the morning after the standard training of the patients lying on the back, right and left side. In the B-scan mode, the size, contour, echogenicity of the kidney structure were studied. In the doppler color mapping mode, the symmetry of blood circulation the kidney segments, the state of venous outflow, blood circulation in the aorta, the state of the renal arteries and veins for the presence of deformations and permeability were evaluated. Pulsed dopplerography measurements included measurements of the renoaortal index, values of peak systolic (Vps) and end-diastolic (Ved) blood velocity, systol-diastolic ratio (S / D), peak index (PI) and resistance index (RI), acceleration time of the circulation (AT) and time-averaged maximum circulation (TAMX) at the level of the trunk of the renal arteries, segmental and interlobar branches.

Checkpoint doppler scanning of renal arteries was performed in patients from 6 months to 4 years after treatment.

Statistical data was processed using Statistica 13.0 (StatSoft, USA, JPZ8041382130ARCN10-J). An analysis of the correspondence of the distribution type of the normal distribution law sign was carried out using the Kolmogorov-Smirnov, Shapiro-Wilk criteria. To compare the average values of the samples, the data of which are distributed according to normal law, the parametric criterion (t-criterion of the Student) was used. Non-parametric methods (Mann-Whitney, Wald-Wolfowitz, Kolmogorov-Smirnov criteria for unbound groups, sign criteria, Wilcoxon for related groups) were used in the description of the distribution of a characteristic that is different from normal or in the case of the description of small samples. To assess the correlation between the cators, the correlation analysis method was used to calculate the Pearson correlation coefficients in normal distribution and Spirman one in other types of distribution. At a value of  $r < 0.25$ , the correlation relationship was regarded as weak, at  $r = 0.25-0.75$  - as a moderate, the correlation coefficient greater than 0.75 was considered as strong. The results obtained in normal distribution were calculated using average and standard deviation ( $M \pm \sigma$ ), when an abnormal distribution - with median, 25 and 75 percentiles (Me (25%, 75%)). Statistically significant in our work were considered results at a level of statistical significance  $p < 0,05$ .

**Results.** The average systolic blood pressure (SBP) index was  $172.5 \pm 21.97$  mm Hg, diastolic blood pressure (DBP) was 100 (90; 110) mm Hg. The level of aldosterone in patients before the treatment was  $388.59 \pm 197.38$  pg / ml, after the treatment -  $125.52 \pm 107.44$  pg / ml.

A comparative analysis of dopplerometric indices before and after the treatment demonstrated statistically significant differences between the Vps, TAMX at the level of the renal artery trunk, PI and AT at the level of the segmental arteries and TAMX at the level of the right-sided arteries of the right kidney (Table 1). The obtained data testify to the normalization of the above-mentioned cators.

Table 1. Doppler sonographic indices of right renal hemodynamics in patients with primary aldosteronism.

The level of branching of the renal artery	Dopplerometric indices	Before the treatment	After the treatment
1	2	3	4
Trunk	Vps, sm/s	$73,33 \pm 27,44^*$	$101,44 \pm 28,39^*$
	Ved, sm/s	$25,77 \pm 6,88$	$32,22 \pm 5,84$
	S/D	$2,81 \pm 0,54$	$3,15 \pm 0,71$
	PI	$1,07 \pm 0,21$	$0,96 \pm 0,21$
	RI	$0,63 \pm 0,07$	$0,67 \pm 0,07$
	AT, s	$0,11 \pm 0,05$	$0,07 \pm 0,02$
	TAMX, sm/s	$41,40 \pm 11,69^*$	$58,18 \pm 12,05^*$

Continuation of table 1.

1	2	3			4		
		Upper segment	Middle segment	Bottom segment	Upper segment	Middle segment	Bottom segment
Segmental	Vps, sm/s	41,33±15,96	52,44±16,47	46,11±16,41	45,55±13,73	55,77±14,02	47,00±10,35
	Ved, sm/s	13,22±4,11	18,33±6,92	15,33±4,41	15,13±5,33	18,89±4,34	16,22±4,17
	S/D	3,20±0,81	3,07±0,37	2,96±0,54	3,08 (2,78; 3,57)	2,95±0,52	2,95±0,49
	PI	1,19±0,33*	1,18±0,18*	1,16±0,30*	0,92±0,19*	0,90±0,13*	0,90±0,19*
	RI	0,67±0,07	0,67±0,04	0,66±0,08	0,65±0,05	0,64±0,09	0,65±0,06
	AT, s	0,11±0,05*	0,10±0,04*	0,10±0,04	0,07±0,01*	0,07±0,01*	0,07±0,01
	TAMX, sm/s	22,63±7,08	30,21±9,30	26,22±8,07	26,85±8,30	32,46±6,91	26,68±5,32
Interlobar	Vps, sm/s	30,55±12,56	31,33±9,64	29,77±11,25	37,77±8,98	33,78±9,03	30,11±6,11
	Ved, sm/s	10,22±3,15	12,33±4,12	10,88±4,81	10,88±2,47	13,66±2,73	10,00 (9,00; 10,00)
	S/D	2,98±0,54	2,75 (2,70; 2,78)	2,88±0,96	2,72 (2,70; 2,91)	2,77±0,39	2,90±0,40
	PI	1,07±0,22	0,89±0,37	1,16±0,45	0,89±0,21	0,86±0,09	0,92±0,13
	RI	0,65±0,06	0,64 (0,63; 0,64)	0,63±0,10	0,64±0,07	0,63±0,05	0,65±0,05
	AT, s	0,11±0,04	0,11±0,05	0,11±0,05	0,07±0,01	0,07±0,01	0,08 (0,07; 0,08)
	TAMX, sm/s	18,12±6,32	18,47±4,60*	17,71±6,36	18,87±3,38	23,10±4,77*	16,70 (16,40; 17,40)
Notice 1. * - statistically significant correlation between the cators (p <0,05).							

From the left kidney, TAMX at the level of the trunk, AT at the level of the segmental arteries and Vps, Ved, S / D, PI, TAMX at the level of the interlobar arteries have been statistically significantly improved. The level of resistance index (RI) of interlobar arteries after the treatment was somewhat increased ( $0.61 \pm 0.06$  vs.  $0.67 \pm 0.03$ ), however, it remained within the reference values (Table 2).

Table 2. Dopplerographic parameters of left kidney hemodynamics in patients with primary aldosteronism.

The level of branching of the renal artery	Dopplerometric indices	Before the treatment			After the treatment		
		3	4	5	6	7	8
Trunk	Vps, sm/s	84,77±47,22			100,55±36,11		
	Ved, sm/s	26,88±8,47			33,11±7,91		
	S/D	2,93±0,76			2,98±0,63		
	PI	1,13±0,31			0,94±0,23		
	RI	0,64±0,07			0,65±0,06		
	AT, s	0,10±0,05			0,08±0,01		
	TAMX, sm/s	40,96±10,54*			59,06±17,61*		

Continuation of table 1.

1	2	3	4	5	6	7	8
		Upper segment	Middle segment	Bottom segment	Upper segment	Middle segment	Bottom segment
Segmental	Vps, sm/s	44,88±15,26	51,33±18,30	40,88±11,70	50,00±13,56	58,33±14,87	43,11±10,71
	Ved, sm/s	16,22±5,95	18,88±5,10	14,22±3,63	16,88±3,88	20,11±3,34	15,33±4,06
	S/D	2,87±0,73	2,68±0,57	2,61±1,00	2,94±0,49	2,90±0,37	2,85±0,50
	PI	1,08±0,21	0,99±0,23	1,13±0,27	0,88±0,13	0,96±0,16	0,92±0,20
	RI	0,64±0,08	0,61±0,07	0,65±0,07	0,65±0,05	0,65±0,04	0,64±0,06
	AT, s	0,12±0,05*	0,19±0,22	0,10±0,05	0,07±0,01*	0,07±0,02	0,06 (0,06;0,07)
	TAMX, sm/s	24,73±6,14	29,88±9,30	22,93±6,44	30,67±7,31	32,00±7,73	24,62±5,97
Interlobar	Vps, sm/s	28,77±4,35	32,33±7,59*	25,44±6,40	32,44±11,18	37,66±10,24*	30,0±8,38
	Ved, sm/s	10,11±3,82	12,33±2,95	8,66±2,17*	11,88±3,06	12,33±3,50	10,88±3,51*
	S/D	3,11±1,14	2,67±0,45*	2,89±0,52	2,56±0,35	3,09±0,36*	2,57 (2,42; 2,88)
	PI	1,17±0,46	0,99±0,20	1,05±0,20*	0,89±0,21	0,94±0,13	0,85±0,15*
	RI	0,64±0,10	0,61±0,06*	0,64±0,06	0,60±0,05	0,67±0,03*	0,63±0,06
	AT, s	0,11±0,03*	0,11±0,05*	0,12±0,04*	0,07±0,01*	0,07±0,02*	0,06±0,01*
	TAMX,sm/s	15,62±2,63	19,21±4,41	14,34±3,09*	19,93±5,37	21,53±4,96	17,90±4,17*

Notice 1. \* - statistically significant correlation between the cators (p <0,05).

The effect of normalization of aldosterone level in blood plasma of patients after the received treatment was analyzed. According to the obtained results of the correlation analysis, the decrease in the level of aldosterone in blood plasma led to an increase in TAMX at the level of the renal artery (r = -0.647, p <0.05), an increase in S / D (r = -0.749, p <0.05 ), RI (r = -0.851, p <0.05, r = -0.651, p <0.05) and decrease in AT at the level of the segmental arteries (r = 0.715, p <0.05), as well as the increase in Ved (r = -0.750, p <0.05; r = -0.791, p = 0.01) at the level of the interlobar arteries (Table 3).

Table 3. Analysis of the correlation between dopplerometric indices of renal hemodynamics and aldosteronemia levels after the treatment.

The level of branching of the renal artery	Dopplerometric indices	Right kidney			Left kidney		
		Upper segment	Middle segment	Bottom segment	Upper segment	Middle segment	Bottom segment
Trunk	Vps		-0,616			-0,138	
	Ved		-0,625			-0,155	
	S/D		-0,098			-0,082	
	PI		0,128			-0,093	
	RI		-0,005			-0,123	
	AT		0,229			0,309	
	TAMX		-0,647*			-0,100	
Segmental	Vps	-0,085	-0,107	-0,115	-0,022	0,188	-0,129
	Ved	0,004	0,201	0,102	0,017	0,066	-0,031
	S/D	0,018	-0,527	0,030	-0,749*	0,208	-0,159
	PI	0,048	-0,124	-0,055	-0,158	0,120	-0,131
	RI	-0,176	-0,376	-0,226	-0,851*	-0,651*	-0,267
	AT	0,715*	0,069	0,469	0,357	0,191	0,050
	TAMX	-0,320	0,022	0,045	-0,083	0,342	-0,135
Interlobar	Vps	-0,060	-0,598	-0,417	-0,266	-0,161	-0,452
	Ved	0,157	-0,750*	-0,198	-0,432	-0,324	-0,791*
	S/D	0,085	0,404	-0,563	0,190	0,506	0,324
	PI	0,066	0,455	-0,351	0,151	-0,379	0,429
	RI	-0,216	0,426	-0,535	0,149	0,587	0,466
	AT	0,269	0,230	0,434	0,006	0,391	0,526
	TAMX	-0,001	-0,613	-0,235	-0,430	-0,277	-0,595

Notice 1. \* - statistically significant correlation between the cators (p <0,05).

An analysis of the correlation connection of the dynamics of blood pressure and intra-liver blood circulation parameters was also conducted. Thus, according to the obtained data, the changes in systolic blood pressure did not affect the intrarenal hemodynamics. However, decrease in diastolic blood pressure led to a decrease in the resistance index at the level of the segmental renal arteries ( $r = 0.681$ ,  $p < 0.05$ ), increase in Ved at the level of interlobar arteries ( $r = -0.723$ ,  $p < 0.05$ ).

**Discussion.** In the scientific community there remains a discussion of changes in renal hemodynamic cies against the background of received treatment in patients with primary aldosteronism.

A more discussed criterion that characterizes the condition of intrarenal hemodynamics is the index of resistance. This parameter was considered to be a predictor of postoperative blood pressure index in patients with primary aldosteronism [12]. According to Sechi et al. the patients showed an increase in the index of resistance compared to the primary level. The increase in the sign of resistance index is observed on average one year after the treatment [13]. At the same time in his work Wu V.C. et al. emphasize that the index of resistance in patients with primary aldosteronism who have aldosterone-producing adenomas is significantly higher before the treatment than in patients suffering from essential hypertension. The results of the study of the resistance index after the treatment illustrated a significant decrease in the rate in the group of patients with primary aldosteronism who had undergone surgical treatment by adrenalectomy, compared to the patients taking spironolactone and the control group even at a similar level of arterial pressure [14].

The data we received cate an increase in the resistance index within the reference indices.

Also, the special difference was the fact that in the preclinical stage, in patients with aldosterone-producing adenomas, a statistically significant lowering of the acceleration of the blood flow time index (AT) was observed compared to the patients with hyperplasia / microadenomas at the level of segmental ( $0.12 \pm 0.04$  versus  $0.08 \pm 0.02$  s,  $p = 0.044$ ) and interlobar ( $0.12 \pm 0.04$  versus  $0.08 \pm 0.02$  s,  $p = 0.029$ ) arteries. This cates a greater effect of aldosterone of produced adenomas compared with hyperplasia or microadenomas on intrarenal hemodynamics in patients with primary hyperaldosteronism.

The obtained results of correlation analysis cate the direct influence of the level of aldosteronemia and the level of diastolic blood pressure on the state of intrarenal hemodynamics after the treatment in patients with primary aldosteronism.

#### **Conclusions.**

1. Ultrasonic doppler scanning of renal arteries can serve as an additional method for assessing the quality of treatment for patients with primary aldosteronism.

2. Complex treatment of patients with primary aldosteronism demonstrates a statistically significant improvement in intrarenal hemodynamics indices.

3. Patients with primary aldosteronism after the treatment have a statistically significant increase in the resistance index within the reference values.

4. The normalization of intrarenal hemodynamic indies is associated with the level of aldosteronemia and diastolic arterial pressure.

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