

## Research Article

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## Predictive Factors for Complete Resolution of Hypertension After Adrenalectomy for Aldosteronoma

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### ABSTRACT

**Introduction:** Primary hyperaldosteronism, 1st cause of secondary hypertension, 2nd cause of hypertension potentially curable by surgery. The objective of this work is to determine the predictive factors for complete resolution of hypertension after adrenalectomy.

**Material:** We conducted a retrospective study of 25 patients with primary hyperaldosteronism operated and followed between 1985 and 2018.

**Results:** Our patients were divided into 16 women and 9 men, mean age 54 years. 40% of our patients were smokers, 36% dyslipidemic, 68% diabetic and 76% had a BMI  $\geq 25$  kg / m<sup>2</sup>. Patients underwent unilateral adrenalectomy, the surgical approach was posterior lumbar in 9 cases and laparoscopic in 16 cases. No per or postoperative complication was noted. The postoperative course was marked by the HTA in 36% of the cases, an improvement in 36% of the cases and persistence in 31% of the cases. We found a significant decrease of the PAS and the PAD at six months of the surgery. The comparative study of the patients whose HTA was cured versus unhealed did not show a statistically significant correlation with the following predictors of healing: young age, female gender, lack of family history of hypertension, adenoma's dimension, the presence of comorbidities including diabetes and dyslipidemia and the average number of antihypertensive treatment. Only the absence of overweight or obesity was a predictor of healing in our series.

**Conclusion:** Knowing the predictive factors of healing aims to pose the operative indication and especially to improve the prognosis of hypertension after surgery by acting on certain modifiable factors.

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### Introduction

Primary hyperaldosteronism (PAH), first cause of secondary arterial hypertension (HTA), second cause of HTA potentially curable by surgery (1), characterized by the association of HTA, hypokalaemia and low plasma renin activity. It is due to hypersecretion of aldosterone either by an adenoma or in the context of hyperplasia.

Untreated PAH is responsible for considerable cardiovascular morbidity. To prevent these complications, it is essential that patients with PAH can be identified, and benefited from a well codified treatment, which depends on the etiology.

adrenalectomy is recommended in case of unilateral adenoma [1].

The objectives of the surgical treatment of PAH are normokalaemia, normotension but also the reduction of the harmful effects of aldosterone on the cardiovascular system [2].

The persistence of hypertension after surgery has raised questions about the indication for surgery during PAH.

In order to establish the indication for surgery, it is necessary to determine the preoperative predictive factors for the cure of arterial hypertension.

### Methods

This is a retrospective, descriptive and analytical study of 25 patients with hypertension secondary to PAH related to lateralized aldosterone secretion, operated on and followed up in the endocrinology department of Charles Nicolle Hospital.

We did not include in our study patients with hypertension related to primary hyperaldosteronism but who did not have surgical treatment (bilateral adrenal hyperplasia, contraindication to surgery, death, patient refusal, etc.) patients operated on but with another cause of adrenal hypertension (pheochromocytoma, independent ACTH Cushing's syndrome, etc.). Were excluded from the study patients lost to follow-up and those who did not consult at least six months or one year after the adrenalectomy and patients with tumors with mixed secretion.

The collection of data was done retrospectively using a form developed in a standardized way in order to collect all the necessary elements taking into account the pre, per and post operative data (demographic, anthropometric, history of hypertension, antihypertensive drugs used, imaging results, various biological parameters, surgical complications, postoperative results for hypertension and hypokalaemia).

The diagnosis of PAH is based on the aldosterone/renin ratio (RAR) measured under standardized conditions (Table 1).

**Table 1: Aldosterone/renin ratio thresholds for the diagnosis of primary hyperaldosteronism**

	Direct renin mIU /l	Direct renin pg / ml= CmlU /L	Plasma renin activity ng / ml/h	Plasma renin activity pmol /l/ min
Aldosterone pmol /L	64	64xC	830	70
Aldosterone pg /ml (= ng /l)	23	23xC	300	25

In patients who are not in one of these two situations, an additional diagnostic step is necessary, in the form of a dynamic confirmatory test. Topographic exploration by imaging was performed in all patients (adrenal ultrasound, adrenal CT, adrenal MRI). Also an assessment of the impact of hypertension was performed in all patients (FO, ECG ± ETT, renal assessment, albuminuria) To determine the factors influencing the surgical result, the patients were divided into two groups: cured hypertension versus hypertension not healed.

Indeed, hypertension is considered cured if the blood pressure figures six months or one year after the adrenalectomy were below 140/90 mm Hg without treatment. Hypertension is considered improved if the blood pressure figures have dropped below 140/90 mmHg under antihypertensive treatment with a reduction in the number and dose of antihypertensive treatments. A treatment failure is defined by a persistence of blood pressure figures above 140/90 mmHg .

**Results**

Our patients are divided into 16 women and 9 men with an average age of 54 years, familial hypertension was present in 13 patients. The demographic, clinical and paraclinical characteristics of the patients are summarized in Table 2.

**Chart 2: The demographic, clinical and paraclinical Characteristics of the patients**

<b>Number of patients studied</b>	<b>25</b>
<b>Average age</b>	<b>54 [ 20; 76]</b>
Gender (male / female)	9(36%) / 16(64%)
<b>BMI ≥ 25kg/m<sup>2</sup></b>	<b>19(76%)</b>
Habits and associated diseases: - Tobacco 40% - Dyslipidemia 36% - Diabetes 68%	
<b>Familial hypertension</b>	<b>13 (52%)</b>
Circumstances of discovery: -HTA + hypokalemia 16 (64%) -Adrenal incidentaloma 8 (32%) -Badly balanced hypertension 1 (4%)	

<b>Seniority of hypertension (years)</b>	<b>7.29 [ 0; 30]</b>
Severity of hypertension ( mmHg ) - Average PAS 163.4 ± 29 -Average PAD 91.2 ± 19.8	
<b>Mean serum sodium mmol /L</b>	<b>140± 3 [ 136; 146]</b>
Mean natriuresis mmol /24h 110.47	
<b>Mean serum potassium mmol /L</b>	<b>3.06 ± 0.92 [1.4;4.5]</b>
Mean kaliuresis mmol /24h	48.57± 16 [ 31; 80]
<b>Mean plasma aldosterone level pg / mL</b>	<b>500.52 ± 516.72 [ 410; 1759]</b>
Aldosterone/ARP coated ratio	>23 [23.71; 700]
<b>Mean adrenal CT size</b>	<b>24.66 mm ± 15.28 [ 10; 70]</b>
Right/left	side 10/13
<b>Unilateral</b>	<b>adrenalectomy 25(100%)</b>
Look first : - posterior lumbar 9 - laparoscopic 16	

BMI: body mass index; HTA: Arterial hypertension; PAS: systolic blood pressure; PAD: Diastolic blood pressure; ARP: Plasma renin activity.

On the therapeutic level, 9 patients (36%) were on monotherapy, 9 patients (36%) were on dual therapy, 3 patients (12%) on triple therapy and 2 patients on quadruple therapy (8%). The treatment was not specified for one patient and hypertension was first discovered in another patient.

Histological examination confirmed the presence of an adrenal adenoma in all cases.

Adrenalectomy allows healing of hypertension (BP<140/90mmhg) without medical treatment in 9 cases (36%). Persistence of hypertension was noted in 7 patients (31%). An improvement in blood pressure observed in 9 cases (36%).

On the hormonal level, the biological cure of PAH based on the dosage of aldosterone and renin in the immediate postoperative period was noted in all the patients who had this hormonal dosage. The evolution of blood pressure profile and serum potassium after adrenalectomy is summarized in Table 3.

**Chart 3: Evolution of blood pressure profile and serum potassium after adrenalectomy**

	Before	After	P-value
Systolic blood pressure (mmHg )	163.0	130.4	0.003
Diastolic blood pressure (mmHg )	91.2	70.8	0.004
Kalemia (mmol /l)	3.06	4.49	0.003

The average number of antihypertensive treatments increased from 3.33 to 2.68 at six months postoperatively, there was no significant drop in antihypertensive treatment (P=0.15).

For the evaluation of the predictive factors of the postoperative evolution of BP in the 25 patients operated on for Conn's adenoma; the two groups were compared: cured hypertension patients versus uncured hypertension. The only predictive factor for healing in our series was the absence of overweight with a BMI  $\leq$  25 Kg/m<sup>2</sup> (Table 4).

**Chart 4: Factors predicting therapeutic response**

	Group A HTA healing (n =9)	Group B Non-healing hypertension (n =16)	P
Age (years)	49.4	52.5	(0.5)ns
Family history of hypertension (%)	16	32	(0.78)ns
Female sex (%)	42.85	57.14	(0.68)ns
SBP ( mmHg )	133.3	145	(0.89)ns
DBP ( mmHg )	86.6	94.2	(0.7)ns
Mean number of preoperative antihypertensive treatments	2.33	1.68	(0.15)ns
Adenoma size (mm)	17.33	18.62	(0.74)ns
BMI $\leq$ 25 (Kg/m <sup>2</sup> )	62.5	36	(0.03)s
Smoking (%)	12	28	(0.6)ns
Diabetes (%)	24	44	(0.9)ns
Dyslipidemia (%)	55.5	44.4	(0.12)ns
Kidney failure (all stages) (%)	8	20	(0.62)ns
LVH (%)	4	24	(0.15)ns

P : significance; ns: not significant; s: significant; PAS: systolic blood pressure; PAD: Diastolic blood pressure; BMI: Body Mass Index; LVH: left ventricular hypertrophy

### Discussion

In our series, hypertension was cured in 36% of patients. It is defined by a normalization of blood pressure figures (BP less than 14/9). By comparing our results with those of studies that have adopted the same healing criteria. The cure rate for hypertension was similar as shown in Table 5 .

**Chart 5: Results of surgery in operated adenomas**

Authors	Case(N)	Healing (%)	BP threshold	Follow-up (months)
Rossi, 2002[3]	30	67	140/90	63
Meria , 2003[4]	212	58	140/90	6-84
Pang , 2007[5]	62	34	140/90	59
Holy, 2017[6]	43	20	140/90	74.4
Our study	25	35	140/90	

Correction of hypokalemia is constant and rapid after adrenalectomy. It occurs within 48 hours of surgery without any potassium supplementation. It reflects the rapid normalization of the plasma aldosterone level after excision of the adrenal adenoma [5,7,8]. Several studies have shown that unilateral adrenalectomy

for Conn's adenoma is followed by normalization of serum potassium in approximately 100% of cases.

In the literature, there are no validated predictors of operative success. However, certain preoperative characteristics seem to predict the effectiveness of the surgical procedure.

Patients under the age of 50 with recent and severe hypertension are good candidates for surgery. After the age of 50, it is prudent to consider surgery only in the event of hypertension resistant to treatment, after having verified the lateralization of aldosterone secretion by catheterization of the adrenal veins, and after having informed the patient of the risk. high rate of surgical failure. Indeed after the age of 50, the incidence of coexisting essential hypertension is high, it does not improve after adrenalectomy. [9,10,11]. In our study, age was not a factor in healing after surgery. This can be explained by the reduced number of our staff and only 8 patients were under 50 years old. According to the latest recommendations [12], surgery is proposed immediately if the age is less than 35 years and the adenoma is unilateral if not for an age greater than 35 years, it is prudent to consider surgery only 'after checking for lateralized aldosterone secretion.

The involvement of sex as a prognostic factor for healing is not clearly established. The majority of authors consider that the female gender is a good prognostic factor for postoperative healing of PAH [13]. In our study, female gender was not a good prognostic factor.

The absence of a family history of hypertension is reported by several studies as a predictive factor for the correction of hypertension after surgery. The family history of hypertension testifies to the coexistence of essential hypertension which does not regress after adrenalectomy [14,15]. In our study, the absence of a family history was not a predictive factor for a good response.

Adipose tissue secretes factors that stimulate aldosterone secretion and increases the sensitivity of vessels to the harmful effects of aldosterone, which increases the morbidity of hypertension and predicts its persistence after adrenalectomy (4) thus a BMI  $\leq$  25 kg /m<sup>2</sup> is a good prognosis factor for healing postoperatively, this was confirmed in our study.

The later the diagnosis of PAH, the lower the probability of recovery from hypertension postoperatively: a duration of hypertension of less than 5 years is one of the most predictive factors of a good clinical response after adrenalectomy [14,15].

The seriousness of the hypertension, or more precisely a preoperative systolic AP higher than 160 mmHg are pejorative factors as for the blood pressure outcome. Severe hypertension related to a very high secretion of aldosterone is associated with a more marked cardiovascular and renal impact, which results in a difficult to control BP even after adrenalectomy [14,15].

By analogy, the need for more than two antihypertensives before surgery testifies to the severe or resistant nature of hypertension in relation to PAH often associated with pre-existing essential hypertension before surgery [14,15]. In our series the mean number of antihypertensive treatment was not correlated with healing.

A deterioration in renal function, defined by a creatinine clearance of less than 90 ml/min, is a poor prognostic factor. Several comparative studies including patients operated on for PAH have shown that cured patients have better creatinine clearance

compared to uncured patients [14,15]. In our series, the prevalence of renal insufficiency was comparable in the two groups.

Several comparative studies between operated, cured and uncured patients have concluded that a size of Conn's adenoma of less than 20 mm is a good prognostic factor [14,15]. In our series, the average size of nodules in patients was 17.29 mm [2-38] and the comparative study of cured versus non-cured patients did not show any significant difference.

Other factors studied such as the side of the lesion, smoking, the presence of diabetes and dyslipidemia and preoperative serum potassium were not correlated with the healing of hypertension in our study. A prospective study of a hundred patients established a prognostic score for resolution of hypertension after adrenalectomy [13] (Table 6).

**Table 6: Hypertension resolution score after adrenalectomy [13]**

Criteria present before adrenalectomy	Number of points
Number of antihypertensive treatments $\leq 2$	2
female sex	1
Duration of hypertension $\leq 6$ years	1
BMI $\leq 25$ kg/m <sup>2</sup>	1

Probability of solving Total points

- Low (27%) 0-1
- Average (46%) 2-3
- High (73%) 4-5

### Conclusion

Knowing the predictive factors of healing makes it possible to properly establish the indication for surgery and above all to improve the prognosis of hypertension after surgery by acting on certain modifiable factors, these actions are summarized in the screening and early diagnosis of hypertension. origin, improvement of blood pressure figures preoperatively by prescribing appropriate antihypertensives, management of associated comorbidities such as diabetes, dyslipidemia and overweight, and programming of the intervention as soon as possible.

### Conflicts of interest

The authors declare that they have no conflicts of interest.

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