Post-saline infusion test aldosterone levels indicate severity and outcome in primary aldosteronism

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Abstract

Objective: The saline infusion test (SIT) is widely used as a confirmatory test for primary aldosteronism (PA). SIT results are judged as follows: post-test aldosterone levels <50 ng/l exclude PA, whereas levels >50 ng/l confirm PA.

We hypothesized that post-SIT aldosterone concentrations indicate the severity of PA and might predict outcome.

Design: The study includes 256 PA patients of the German Conn's Registry who prospectively underwent SIT. The data of 126 patients with complete follow-up of 1.2 ± 0.3 years after diagnosis were analyzed. The patients were divided into two groups with post-SIT aldosterone levels of 50–100 ng/l (group 1; $n=38$) and of >100 ng/l (group 2; $n=88$).

Results: Patients in group 2 had a significantly shorter duration of hypertension (7.5 vs 11.7 years (median), $P=0.014$), higher systolic blood pressure (BP; 151 ± 16 vs 143 ± 17 mmHg, $P=0.036$), lower serum potassium (3.3 ± 0.6 vs 3.5 ± 0.4 mmol/l, $P=0.006$), higher 24-h urine protein excretion (7.4 vs 5.4 mg/dl (median), $P=0.012$), and were more often female ($P=0.038$). They showed more often unilateral disease ($P<0.005$) with larger tumors (14 ± 10 vs 7 ± 10 mm, $P=0.021$), underwent more often adrenalectomy (75% vs 37%, $P<0.005$), required a lower number of antihypertensive drugs after adrenalectomy (1.2 ± 1.2 vs 2.5 ± 1.4 , $P=0.001$), had a faster normalization of urinary protein excretion (with medical treatment $P=0.049$; with Adx $P<0.005$) at follow-up, and more frequently underlying well-characterized mutation ($P=0.047$).

Conclusions: PA patients with post-SIT aldosterone levels of >100 ng/l have a more rapid development of PA caused more frequently by unilateral disease with larger aldosterone-producing adenomas. However, this group of patients may have a significantly better outcome following specific treatment.

European Journal of
Endocrinology
(2015) 172, 443–450

Introduction

Primary aldosteronism (PA) is the most common form of secondary hypertension and affects up to 10% of all hypertensive patients (1). Patients with PA have an increased risk of developing relevant comorbidities, e.g. vascular, cardiac, or cerebrovascular morbidities and renal insufficiency compared with other hypertensive patients

(2, 3, 4, 5, 6, 7). Therefore, it seems mandatory to detect early patients with PA. The aldosterone-to-renin ratio (ARR) is recommended for screening patients with suspected PA (8). The guidelines of the Endocrine Society recommend that patients with a positive ARR measurement should undergo any of four confirmatory tests to

confirm or exclude the diagnosis of PA (8). However, up to date there is no gold-standard confirmatory test for PA because all test performances have been evaluated only retrospectively, in relatively small series of patients and only in comparison with other tests rather than toward a conclusive diagnosis of PA (8). In Germany, the most widely used confirmatory test due to practicability, costs, and compliance is the saline infusion test (SIT). For the SIT post-infusion plasma aldosterone levels of <50 ng/l largely exclude the diagnosis of PA, whereas levels of >100 ng/l confirm PA. Values between 50 and 100 ng/l are often described as 'indeterminate' in older studies (9, 10, 11, 12), or interpreted as a mild or early form of PA.

To further investigate clinical, biochemical, and radiological features in PA with modest (post-SIT aldosterone levels of 50–100 ng/l) and with more substantial elevation of aldosterone levels (post-SIT >100 ng/l), we analyzed data from the German Conn's Registry, which was founded in 2006 to evaluate the diagnosis, treatment, and outcome of PA in Germany. Owing to the persistent lack of outcome data in PA patients, we were especially interested in the clinical outcome of these two groups with regard to adrenalectomy or medical treatment. We hypothesized that post-SIT aldosterone concentrations indicate the severity of PA and might predict outcome.

Subjects and methods

Design and patients

The German Conn's Registry (www.conn-register.de) is a multi-center database analyzing comorbidities and long-term outcome of patients with PA (4, 13, 14). Since the initiation of the prospective phase in October 2008, all patients actively treated within the centers were entered in a common database after pseudonymization (15). The Ethics Committees of the University of Munich and of the participating centers approved the protocol. Data protection laws were strictly adhered to.

Clinical data at time of diagnosis were extracted from patients' charts including laboratory test results, initiation of mineralocorticoid antagonist treatment, surgical treatment, cardiovascular comorbidities, and BMI. Blood was generally drawn in the fasting state. Every 6 and 12 months the patients were seen for follow-up visits including a clinical examination, laboratory investigation, and cardiovascular examinations.

The diagnostic criteria for PA in this study were chosen according to the Endocrine Society practice guidelines (8). All patients included had an elevated ARR (in sitting

position between 0800 and 1000 h) and an abnormal confirmatory test (4, 16). Adjustment of medication before screening and confirmation was performed whenever possible, using β -blockers, central α -2 agonists, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, diuretics withdrawn for at least 1 week, and mineralocorticoid antagonists at least for 4 weeks. The diagnosis of PA was centrally verified by review of all available data.

In the prospective phase of the German Conn's Registry, 256 PA patients underwent a recumbent SIT as confirmatory test. SIT was carried out with a 4-h saline infusion (2 l i.v.) in supine position between 0800 and 1200 h. Cortisol levels decrease during testing served as validation to exclude stress-related stimulation of aldosterone. A post-SIT aldosterone level >50 ng/l confirmed the diagnosis of PA.

Only patients with a complete data set at diagnosis and at follow-up were included. Sufficient data coverage was available for 126 prospectively recruited patients, who were included in the final analysis.

Subtype differentiation between aldosterone-producing adenoma (APA) and bilateral adrenal hyperplasia was based on adrenal imaging (computed tomography or magnetic resonance imaging) and on adrenal vein sampling (AVS), the latter performed in 94% of the patients included ($n=118$).

AVS was carried out after 2–3 h of resting in supine position between 0800 and 1200 h as described previously (17). Selective AVS was assumed for the purpose of this study, if cortisol of the adrenal vein was 100% higher than cortisol in the inferior vena cava (cortisol in adrenal vein/cortisol in inferior vena cava ≥ 2.0). We used a lateralization index in AVS of ≥ 4 to define unilateral aldosterone secretion.

AVS was successful in 94% of patients ($n=111$). For further analysis, we distinguished between two patient groups in our prospective cohort: patients who had a post-SIT aldosterone level between 50 and 100 ng/l (group 1), and patients with a post-SIT aldosterone level >100 ng/l (group 2).

Eighty patients in the whole cohort underwent adrenalectomy: 46 tumor samples from two centers (Munich and Berlin) were available for DNA isolation and sequencing. Tumor DNA was extracted and analyzed as part of recently published studies by Beuschlein *et al.* (18) and by Fernandes-Rosa *et al.* (19).

We defined the outcome as follows:

Cured (adrenalectomy patients only) = serum potassium >3.4 mmol/l and systolic blood pressure (BP)

<140 mmHg and diastolic BP <90 mmHg and no antihypertensives.

Controlled (medically treated patients only)=serum potassium >3.4 mmol/l and systolic BP <140 mmHg and diastolic BP <90 mmHg and on therapy with mineralocorticoid (MR)-antagonists, but no other antihypertensives §.

Significantly improved=normokalemia and systolic BP decrease by ≥ 10 mmHg and decrease of antihypertensives by ≥ 1 §.

Slightly improved=normokalemia and (systolic BP decrease by ≥ 10 mmHg or decrease of antihypertensives by ≥ 1 §).

No improvement=persistent hypokalemia or no BP improvement according to the above criteria. §, MR antagonist was not counted as an antihypertensive.

Statistical analyses

Variables were assessed for normality by Kolmogorov–Smirnov test. Results are expressed as mean $\pm$ s.d. if not stated otherwise. Differences between the two groups were assessed using Student's *t*-test for normally distributed variables and Mann–Whitney *U* test for non-normally distributed variables. For paired data and for non-normally distributed variables, we used paired Wilcoxon's test.

For categorical variables and unpaired data we used χ^2 -test/Fisher's exact test and for categorical variables and paired data we used McNemar test. A *P* value <0.05 was considered as significant. Statistical analysis was carried out using IBM SPSS Statistics 20.

Results

Of the 126 PA patients included in this analysis, 38 PA patients had a post-SIT aldosterone level between 50 and 100 ng/l (group 1) and 88 PA patients a post-SIT aldosterone >100 ng/l (group 2). Patients of group 2 were significantly more often hypokalemic, had hypertension for a shorter duration, showed higher systolic BP, and a higher proteinuria at time of diagnosis (Table 1). Group 2 contained a higher proportion of female patients than group 1 and showed a significant higher rate of unilateral aldosterone secretion resulting in a higher rate of adrenalectomies (Table 2). In group 1 only 14 patients (37%) had unilateral disease and were adrenalectomized. In comparison with the 66 patients (75%) of group 2 who underwent adrenalectomy, patients of group 1 were significantly older, had lower potassium levels, and more antihypertensive drugs at follow-up (1.2 ± 0.3 years) (Table 3). The tumor size on imaging was significantly larger in group 2 (Table 3).

Table 1 Clinical and biochemical parameters of 126 prospective PA patients at diagnosis (baseline) depending on post-SIT aldosterone values. Values are means $\pm$ s.d. (median).

	Group 1 (n=38)	Group 2 (n=88)	P value
Duration of hypertension (years)	16.4 $\pm$ 12.5 (11.7)	11.3 $\pm$ 11.4 (7.5)	0.014 ^a
Age at PA diagnosis (years)	53.9 $\pm$ 11.3	50.4 $\pm$ 12.4	0.142 ^b
Male/female	29 (76%)/9 (24%)	50 (57%)/38 (43%)	0.038
24-h systolic BP (mmHg)	143 $\pm$ 17	151 $\pm$ 16	0.036 ^b
24-h diastolic BP (mmHg)	91.0 $\pm$ 11.1	93.7 $\pm$ 13.5	0.345 ^b
Aldosterone (ng/l)			
Pre-test	183 $\pm$ 68.3 (174)	304 $\pm$ 189 (247)	<0.005 ^a
Post-test	72.5 $\pm$ 15.0 (72.3)	220 $\pm$ 120 (178)	<0.005 ^a
Renin (ng/l)			
Pre-test	4.56 $\pm$ 3.62 (3.90)	4.45 $\pm$ 5.08 (2.40)	0.405 ^a
Post-test	3.07 $\pm$ 2.39 (2.76)	3.19 $\pm$ 4.07 (1.80)	0.361 ^a
ARR			
Pre-test	81.7 $\pm$ 73.6 (41.9)	184 $\pm$ 312 (87.8)	0.009 ^a
Post-test	44.0 $\pm$ 40.3 (26.1)	176 $\pm$ 251 (117)	<0.005 ^a
GFR (MDRD) (ml/min per 1.73 m ²)	91.5 $\pm$ 24.4	87.0 $\pm$ 23.2	0.335 ^b
Serum creatinine (mg/dl)	0.91 $\pm$ 0.27 (0.90)	0.91 $\pm$ 0.31 (0.80)	0.587 ^a
Serum potassium (mmol/l)	3.5 $\pm$ 0.4	3.3 $\pm$ 0.6	0.006 ^b
Protein in 24-h urine (mg/dl)	19 $\pm$ 63 (5.40)	38 $\pm$ 91 (7.40)	0.012 ^a
No. of antihypertensives	1.7 $\pm$ 1.2	2.0 $\pm$ 1.1	0.299 ^b
BMI (kg/m ²)	29 $\pm$ 5	29 $\pm$ 5	0.648 ^b

Group 1, post-SIT aldosterone 50–100 ng/l; group 2, post-SIT aldosterone > 100 ng/l; BP, blood pressure; ARR, aldosterone-to-renin ratio; GFR, glomerular filtration rate.

^aMann–Whitney *U* test.

^bStudent's *t*-test.

Table 2 Baseline features of 126 prospective PA patients depending on post-SIT aldosterone values.

	Group 1 (n=38)	Group 2 (n=88)	P value ^a
Successful AVS	35 (92%)	76 (86%)	0.001
Bilateral/unilateral disease	19 (50%)/ 16 (42%)	18 (21%)/ 58 (66%)	
Adrenalectomy, yes/no	14 (37%)/ 24 (63%)	66 (75%)/ 22 (25%)	<0.005

Group 1, post-SIT aldosterone levels of 50–100 ng/l; group 2, post-SIT aldosterone levels of > 100 ng/l; AVS, adrenal vein sampling.

^a χ^2 test.

Twenty-four patients of group 1 and 22 patients of group 2 showed bilateral disease or refused adrenalectomy ($n=5$) and, therefore, were put on medical therapy. At follow-up, medically treated patients of group 1 showed lower aldosterone levels but a similar ARR as group 2. Protein excretion of group 2 was reduced on medical therapy compared with the time at diagnosis, but was still higher than that of group 1 (Table 4).

BP normalization, normokalemia, and reduction in antihypertensive medication were more often achieved in group 2 than in group 1 (Fig. 1). Patients on medical therapy reached the outcome ‘controlled’ or ‘significantly improved’ only in 25 or 27% (groups 1 and 2 respectively). Of patients who underwent adrenalectomy, significantly ($P=0.038$) more patients showed no improvement in

group 1 compared with group 2 (Fig. 1). The overall outcome was significantly better ($P=0.01$) in patients who underwent adrenalectomy compared with patients on medical therapy. ARR at screening and post-SIT aldosterone showed similar strength as predictors regarding outcome ($r=-0.188$, $P=0.045$ and $r=-0.182$, $P=0.041$ respectively). Post-SIT aldosterone levels remained significant ($P=0.046$) after correction for main confounding variables (age, duration of hypertension, and BP).

Forty-six tumor samples from 80 adrenalectomies (58%) were available (eight from group 1 and 38 from group 2). The frequency of well-defined somatic mutations was significantly higher ($P=0.047$) in group 2 (22 of 38; 58%) than in group 1 (one of eight; 13%). In group 1, only one tumor revealed a mutation in the *KCNJ5* gene, whereas 17 tumors of group 2 showed a mutation in the *KCNJ5* gene (45%), one in the *CACNA1D* gene (3%), three in the *ATP1A1* gene (8%), and one in *ATP2B3* gene (3%).

Discussion

Mulatero *et al.* (20) had demonstrated that the SIT is a reasonably reliable alternative to the more time demanding and expensive fludrocortisone suppression test for the confirmation of PA, showing a specificity of 84% and sensitivity of 88% with a cutoff value of 50 ng/l.

Table 3 Clinical and biochemical parameters of 80 prospective PA patients 1.2±0.3 years after adrenalectomy (follow-up) depending on post-SIT aldosterone values at diagnosis. Values are means±s.d. (median).

After ADX	Group 1 (10 m/4 f)	Group 2 (37 m/29 f)	P value
Age at follow-up visit	58±12	50±12	0.032 ^a
Aldosterone (ng/l)	90±73 (68)	71±46 (55)	0.536 ^b
Renin (ng/l)	39±77 (10)	20±24 (10)	0.438 ^b
ARR	35±75 (12)	10±15 (6)	0.244 ^b
24-h systolic/diastolic BP (mmHg)	133/84±17/10	134/83±12/9	0.873/0.763 ^a
GFR (MDRD) (ml/min per 1.73 m ²)	77±24	75±23	0.800 ^a
Serum creatinine (mg/dl)	1.1±0.4	1.1±0.3	0.720 ^a
Serum potassium (mmol/l)	4.0±0.4	4.3±0.5	0.027 ^a
Protein in 24-h urine (mg/dl)	4.9±2.1 (5.0)	5.6±3.2 (5.0)	0.788 ^b
No. of antihypertensives	2.5±1.4	1.2±1.2	0.001 ^a
Tumor size according to pathological report (mm)	16±11 ($n=10$); $n=1$ NH; $n=3$ ND	25±18 ($n=49$); $n=1$ NH; $n=16$ ND	0.135 ^a
Tumor size according imaging (mm)	7±10 ($n=12$); $n=2$ ND	14±10 ($n=64$); $n=2$ ND	0.021 ^a
No. of patients with mutation	1 of 8	22 of 38	0.047 ^c
<i>KCNJ5</i>	1	17	
<i>CACNA1D</i>	0	1	
<i>ATP1A1/ATP2B3</i>	0/0	3/1	

Group 1, post-SIT aldosterone levels of 50–100 ng/l; group 2, post-SIT aldosterone levels of > 100 ng/l; ARR, aldosterone-to-renin ratio; BP, blood pressure; GFR, glomerular filtration rate; NH, nodular hyperplasia; ND, no data available.

^aStudent's *t*-test.

^bMann–Whitney *U* test.

^cFisher's exact test.

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Table 4 Clinical and biochemical parameters of 46 prospective PA patients after 1.2 ± 0.3 years of medical therapy (follow-up) depending on post-SIT aldosterone values at diagnosis. Values are means $\pm$ s.d. (median).

Medical therapy	Group 1 (19 m/5 f)	Group 2 (13 m/9 f)	P value
Age at follow-up visit	53 $\pm$ 11	56 $\pm$ 13	0.490 ^a
Aldosterone (ng/l)	194 $\pm$ 119 (151)	434 $\pm$ 348 (354)	0.003 ^b
Renin (ng/l)	21 $\pm$ 27 (10)	41 $\pm$ 71 (13)	0.425 ^b
ARR	34 $\pm$ 43 (13)	35 $\pm$ 36 (25)	0.620 ^b
24-h systolic/diastolic BP (mmHg)	138/84 $\pm$ 15/6 (136/83)	138/86 $\pm$ 26/16	0.562/0.615 ^a
GFR (MDRD) (ml/min per 1.73 m ²)	80 $\pm$ 22	73 $\pm$ 27	0.277 ^a
Serum creatinine (mg/dl)	1.0 $\pm$ 0.4 (1.00)	1.1 $\pm$ 0.3 (0.9)	0.938 ^b
Serum potassium (mmol/l)	4.1 $\pm$ 0.5	4.1 $\pm$ 0.5	0.867 ^a
Protein in 24-h urine (mg/dl)	5.6 $\pm$ 2.7 (5.1)	11.7 $\pm$ 12.9 (7.0)	0.032 ^b
No. of additional antihypertensives ^c	1.7 $\pm$ 1.0	1.9 $\pm$ 1.4	0.653 ^a
MR antagonist (daily dose in mg)			
Spironolactone	43 $\pm$ 19 (n = 18)	49 $\pm$ 22 (n = 20)	0.355 ^a
Eplerenone	80 $\pm$ 45 (n = 5)	– (n = 0)	–
Dose unknown (n)	1	2	

Group 1, post-SIT aldosterone levels of 50–100 ng/l; group 2, post-SIT aldosterone levels of > 100 ng/l; ARR, aldosterone-to-renin ratio; BP, blood pressure; GFR, glomerular filtration rate.

^aStudent's *t*-test.

^bMann–Whitney *U* test.

^cMR antagonist was not counted as an antihypertensive.

Accordingly, SIT is the most widely used confirmatory test for PA in many countries including Germany. In addition to the SIT, the patients in our prospective cohort underwent AVS to differentiate between uni- and bilateral disease. Thereby, we were able to show that 42% of patients with a post-SIT aldosterone levels between 50 and 100 ng/l had unilateral disease. Furthermore, our analysis indicates that patients with post-SIT aldosterone levels of >100 ng/l had more severe PA with faster development of hypertension, higher systolic BP, lower serum potassium, and higher 24-h urine protein excretion at diagnosis. Importantly, in this group, the percentage of patients with unilateral PA was significantly higher than that in the group with post-SIT aldosterone levels of 50–100 ng/l. This is in accordance to a previous small study showing that patients with APA displayed a smaller reduction in aldosterone levels in SIT compared with patients with bilateral adrenal hyperplasia (20). Another study had shown that patients with higher preoperative BP experienced a greater decrease in BP after adrenalectomy (21).

We found more patients in the group with post-SIT aldosterone level > 100 ng/l, who were tested positive for somatic mutations in the removed APA compared with operated patients with a post-SIT aldosterone level of 50–100 ng/l. Previously published data have demonstrated that patients with *KCNJ5* mutations are more frequently female and are diagnosed at a younger age (19, 22). This is in accordance with our cohort data, showing a higher percentage of female patients in the group with post-SIT

aldosterone level > 100 ng/l, and a higher percentage of *KCNJ5* mutations.

Interestingly, patients with post-SIT aldosterone level of > 100 ng/l, despite their more severe form of hypertension, responded better to specific therapy than those with a post-SIT aldosterone level of 50–100 ng/l: specifically, 1 year following therapy, they had faster normalization of urinary protein excretion and a better outcome, as defined by serum potassium and BP normalization and no or reduced antihypertensive drugs. For patients with post-SIT aldosterone levels of 50–100 ng/l, at least one of three parameters improved following adrenalectomy in 50% (vs 77%) and after medical therapy in 71% (vs 82%) respectively. Accordingly, the cure rate following adrenalectomy (defined as serum potassium > 3.4 mmol/l + BP < 140/90 mmHg + no antihypertensive drugs) was only 32% in the high aldosterone group and 7% in the low aldosterone group respectively. Similarly, a controlled status after medical therapy (defined as serum potassium > 3.4 mmol/l + BP < 140/90 mmHg + on therapy with MR-antagonists, but no other antihypertensive drugs) was achieved in 14% in the high aldosterone group and 4% in the low aldosterone group respectively. The better outcome in the group with post-SIT aldosterone levels of > 100 ng/l might be mostly driven by the higher rate of *KCNJ5* mutations with higher aldosterone levels, which generally show a better surgical outcome. This might also explain the finding of a recent study describing a better clinical course in patients with the presence of an adenoma rather than hyperplasia (23).

Figure 1

Outcome data in 126 PA patients with adrenalectomy (A) or medical therapy (B) depending on post-SIT aldosterone values at diagnosis. Group 1 (black bars), post-SIT aldosterone levels of 50–100 ng/l and group 2 (white bars), post-SIT aldosterone levels of > 100 ng/l. Cured (adrenalectomy patients only) = serum potassium > 3.4 mmol/l and systolic blood pressure < 140 mmHg and diastolic blood pressure < 90 mmHg and no antihypertensives. Controlled (medically treated patients only) = serum potassium > 3.4 mmol/l and systolic blood pressure < 140 mmHg and diastolic blood pressure < 90 mmHg and on therapy with MR-antagonists, but no other antihypertensives §. Significantly improved = normokalemia and systolic blood pressure decrease by ≥ 10 mmHg and decrease of antihypertensives by ≥ 1 §. Slightly improved = normokalemia and systolic blood pressure decrease by ≥ 10 mmHg or decrease of antihypertensives by ≥ 1 §. No improvement = persistent hypokalemia or no blood pressure improvement. §, MR antagonist was not counted as an antihypertensive.

A recent study (24) investigating unilateral adrenalectomy in bilateral primary hyperaldosteronism has shown that hypertension was cured in 15% of patients and improved in 20%. Also the proportion with controlled hypertension was significantly higher after adrenalectomy (65%) than before (25%). This suggests that unilateral adrenalectomy might be beneficial in some patients with bilateral disease (24), which should not be

ruled out *per se* regarding the rather disappointing outcome data in our cohort.

Our cure/controlled rate is similar to that of a small study with 24 PA patients who showed a cure rate of 33% after adrenalectomy (25). Possible reasons for the overall rather low cure rate in our study may be the long-lasting insufficiently treated hypertension due to delayed diagnosis in patients with PA. Other studies, which reported a better outcome (23), usually used only one outcome parameter, e.g. BP, and used often less strict definitions for 'cure' such as a BP < 160/95 mmHg (26). In an Italian study with 50 patients who underwent adrenalectomy, the BP outcome was 30% in remission, 53% markedly improved, and 18% showing mild improvement (27). These outcome rates might again be better than in our series due to the shorter duration of hypertension and due to the less stringent definition of outcome.

A recent paper by Steichen *et al.* (28) has summarized the studies on outcome of adrenalectomy in PA patients and calculated a pooled cure rate of 42% regarding BP as the only outcome parameter, and with significant heterogeneity across the series. In fact, hardly any study has provided a combined outcome analysis of BP and antihypertensive medication. However, the authors pointed out that adrenalectomy usually results in a significant decrease in systolic BP and in the number of antihypertensive medications prescribed (29). Steichen *et al.* (28) analyzed adrenalectomy series in PA patients also regarding factors influencing the outcome, which were also highly variable among the studies. However, factors which seem to have a significant negative effect on the outcome were male sex, older age, family history of hypertension, longer duration of hypertension, higher preoperative BP, more drug classes, higher BMI, higher serum potassium concentrations, lower estimated glomerular filtration rate, or higher 24-h urinary aldosterone-to-/active renin ratio (21, 28). In our study, we could confirm that sex, age, and duration of hypertension influence outcome; however, a higher preoperative BP was not relevant in our cohort. Our data suggest that low post-SIT aldosterone levels (50–100 ng/l) may be an additional indicator of less successful outcome. However, this needs to be validated in other cohorts. Sawka *et al.* (30) suggested that a higher pre-operative ARR might result in a better outcome after adrenalectomy. This is in accordance with our finding showing higher ARR in the group with post-SIT aldosterone levels of > 100 ng/l.

The only prediction model validated to date is a study with 100 patients who underwent adrenalectomy for PA with validation in an independent series of 67 patients

from another center (31). In this study, a high percentage of patients continued to require antihypertensive medications to control their BP. The best predictors for cure of hypertension following adrenalectomy were a number of antihypertensive medications of ≤ 2 , a BMI ≤ 25 kg/m², duration of hypertension ≤ 6 years, female sex (31), and age (2, 30). We confirm in our study that male PA patients had a poorer outcome than female patients. Nevertheless, the underlying causes of persistent hypertension after PA therapy remain controversial (28). One additional aspect might be that a patient with treated PA is not immune to essential hypertension.

In conclusion, PA patients with post-SIT aldosterone levels of > 100 ng/l have a more rapid development of PA caused more frequently by unilateral disease with larger APAs. They showed a better outcome regarding BP, potassium normalization, and reduction in the number of antihypertensive drugs. We suggest that the post-SIT aldosterone level is a predictor for the remission probability of PA post adrenalectomy.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding

This research was supported by the Else Kröner-Fresenius-Stiftung, Germany.

Acknowledgements

The authors are indebted to Kathrin Zopf and Christiane Friedrich, Clinical Endocrinology, Charité Campus Mitte, University Medicine Berlin, for their help with patients' recruitments. The authors wish to thank Susanne Schmid, Friederike Konrad, Nina Nirschl, and Brigitte Mauracher for excellent assistance. We also express our gratitude to the other centers of the study for the collaboration, especially ENS@T centers and Maria-Christina Zennaro, INSERM, UMRS_970, Paris Cardiovascular Research Center, Paris, France.

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Received 21 November 2014

Revised version received 18 January 2015

Accepted 28 January 2015