Medizinische Klinik - Innenstadt
Department of Internal Medicine
Ziemssenstr. 1, 80336 Munich

Conference Program and Abstracts

Progress in Primary Aldosteronism 2

From basic research to clinical evidence

May 4th-6th, 2011

Munich, Carl Friedrich von Siemens Stiftung
Südliches Schlossrondell 23
D-80638 Munich

Progress in Primary Aldosteronism 2

Deutsches Conn-Register
Else Kröner-Fresenius Conn-Register

From basic research to clinical evidence

We gratefully acknowledge

the support of this symposium received from

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Carl Friedrich von Siemens Stiftung

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Welcome

May 4, 2011

Dear Participants of the 2nd Symposium on Progress in Primary Aldosteronism,

Primary Aldosteronism has been a topical issue since the discovery that it represents the most frequent secondary cause of hypertension. Although there has been significant progress in diagnosis and treatment, there are still many fields of uncertainty. After having hosted the highly stimulating symposium *Progress in Primary Aldosteronism 1* in 2009 we are most grateful to announce the follow-up meeting PIPA 2 which will take place in the same location and will have an international faculty with experts from all areas.
This symposium will have a special focus on adrenal vein sampling. It starts with a consensus statement workshop on Wednesday afternoon and continues with a Thursday afternoon session with experts around the world. Additional topic sessions cover genetics and pathophysiology as well as case detection and consequences of aldosterone excess.

We warmly welcome all participants here in Munich and expect a stimulating conference.

Sincerely,

Martin Reincke Felix Beuschlein

for the Organising Committee

Progress in Primary Aldosteronism 2

From basic research to clinical evidence

Content

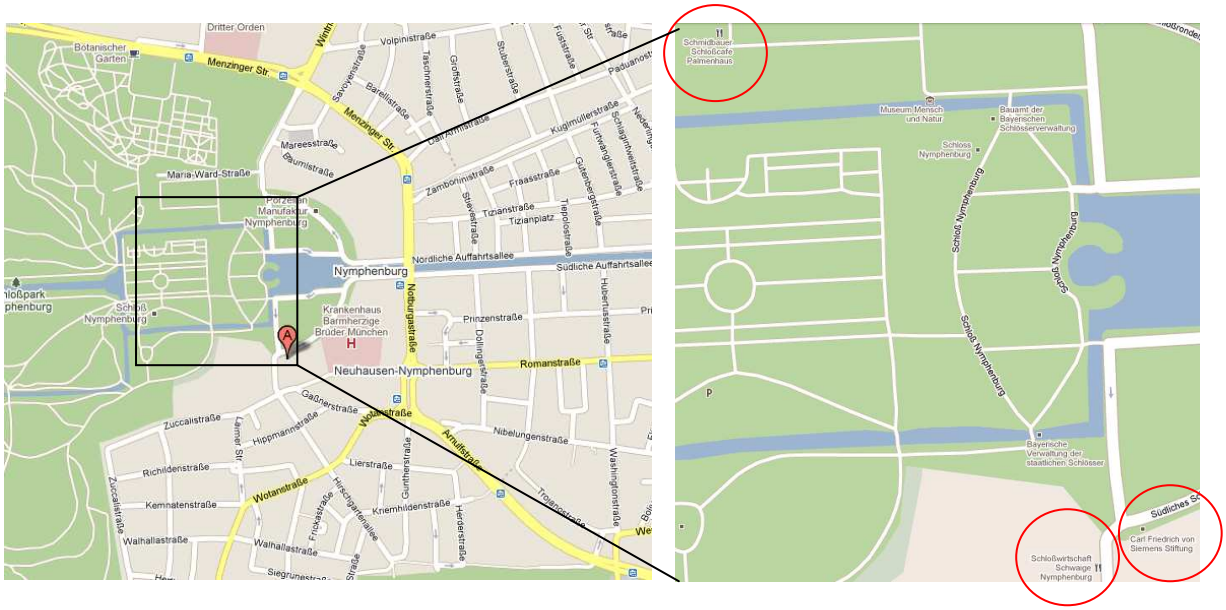
Directions

Direction from the airport to the conference:

Take the suburban train S8 to the central station (Hauptbahnhof).
Than change to the tramway 17 direction Amalienburgstr. to the station Romanplatz.

Conference Address

A: Carl Friedrich von Siemens Stiftung
Südliches Schlossrondell 23
80638 Munich
☎ +49 89 1780 330



Social Program

Wednesday, May 4th 2011: Dinner in the Schlosswirtschaft Schwaige
Schloss Nymphenburg 30, 80638 Munich
Walking time from the Symposium: 3 min.
☎ +49 89/12 0208 90

Thursday, May 5th 2011: Dinner in the Schlosscafé im Palmenhaus
Schloss Nymphenburg, Entry 43, 80638 Munich
Walking time from the Symposium: 10 min.
☎ +49 89/17 53 09

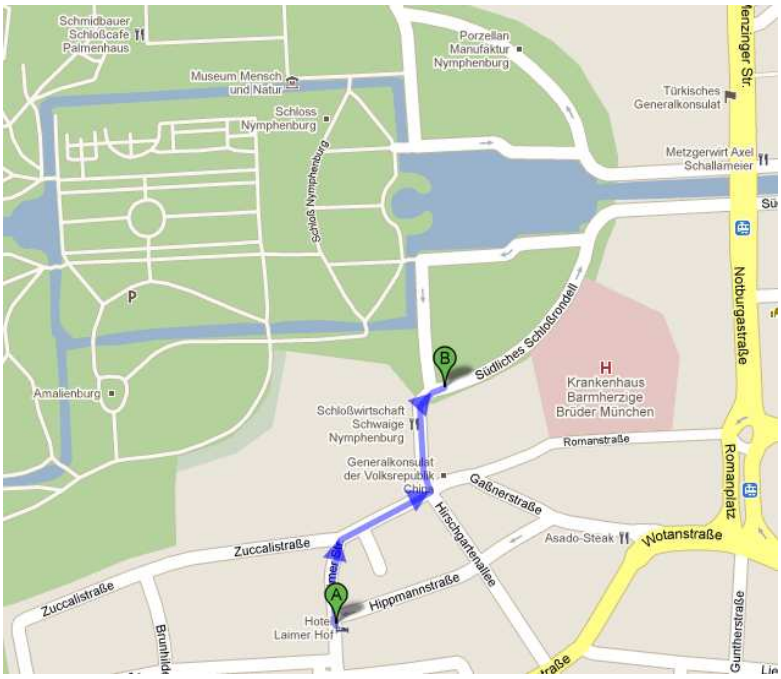
Hotels:

Hotel Laimer Hof
Laimer Str. 40
80639 Munich
☎ +49989/1780380

Hotel Aida
Verdistr. 9
81247 Munich
☎ +4989/8911550

Hotel Kriemhild
Guntherstr. 16
80639 Munich
☎ +4989/1711170

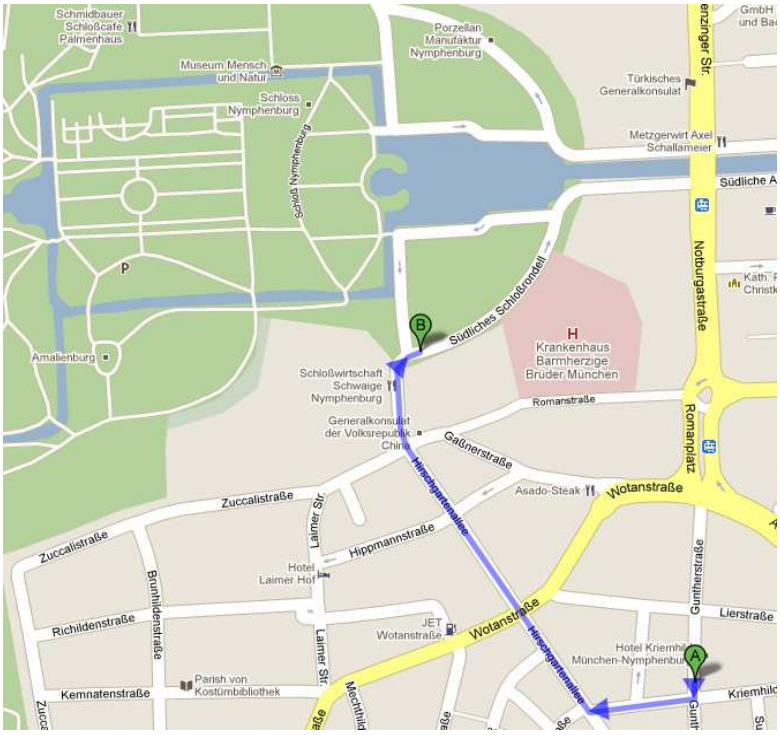
Carathotel
Lindwurmstr. 13
80337 Munich
☎ +4989/230380



A: Hotel
Laimer Hof

B: Symposium

Walking time: 5 min.



A: Hotel Kriemhild

B: Symposium

Walking time: 10 min.

tramway station Amalienburgstr.

A: Hotel Aida

B: Symposium

Walking time: 30 min. (blue line)

Or: take the tramway 17 direction Effnerplatz from the station Amalienburgstraße to the station Schloss Nymphenburg

tramway station Schloss Nymphenburg

Progress in Primary Aldosteronism 2

Deutsches Conn-Register
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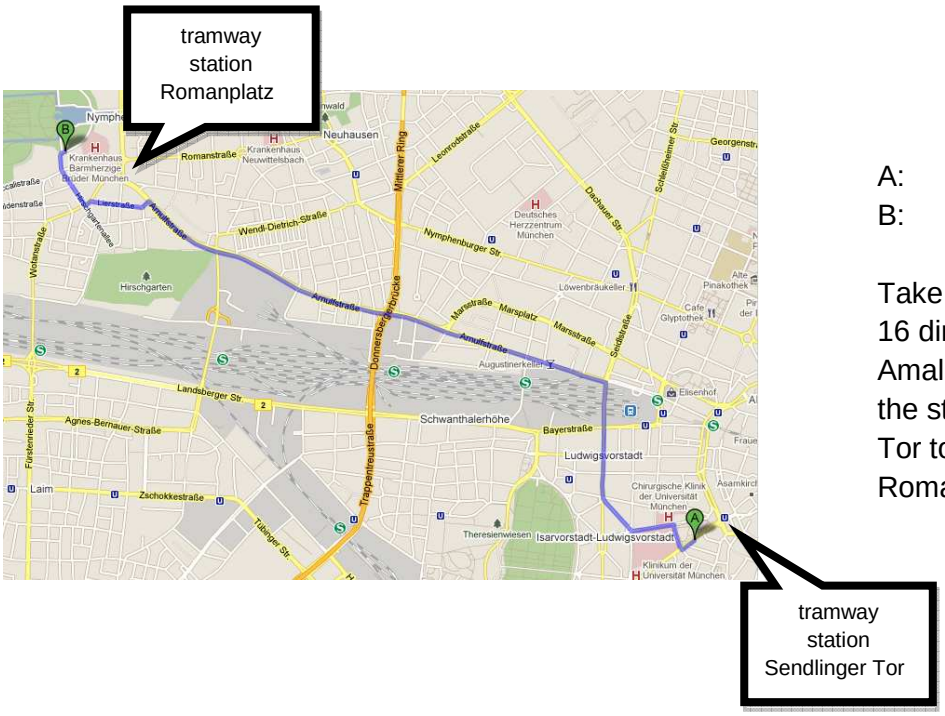
From basic research to clinical evidence



A: Carathotel
B: Symposium

Take the tramway 16 direction Amalienburgstr from the station Sendlinger Tor to the station Romanplatz

If you are lost, please call:

Dr. med Evelyn Fischer
☎ +49176/211 355 04

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Emergency call: 112
Police: 110

Conference Program

Progress in Primary Aldosteronism 2

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Wednesday, May 4th 2011

16:00-19:00 **Workshop *Consensus Statement Adrenal Vein Sampling***

Chairs: B. Allolio, Würzburg; M. Reincke, Munich

19:00 **Dinner in the Schlosswirtschaft Schwaige**

Thursday, May 5th 2011

08:30 **Registration**

09:00 **Welcome Address**

Martin Reincke, Munich

09:15 **The Endocrine Society Practice Guidelines revisited: Need for a change?**

John Funder, Clayton, Victoria, Australia

<u>Session I</u> Progress in Genetics of PA

Chairs: M. C. Zennaro; E. Gomez-Sanchez

09:45 **Topic A: Exome Sequencing in FH 2**

Thomas Meitinger, Tim Strom, Munich

10:05 **Topic B: New Mouse Models**

Felix Beuschlein, Munich

10:25 **Topic C: Familial Aldosteronism Type 3 : What is new?**

David Geller, New Haven, USA

10:45 *Coffee break*

<u>Session II</u> Pogress in Pathophysiology of PA

Chairs: M. Quinkler; P. Mulatero

11:15 **Topic A: Transcriptome Studies in PA**

Maria-Christina Zennaro, Paris

From basic research to clinical evidence

11:35 **Topic B: Plasticity of Aldosterone Production: Role of the Beta-Catenin Pathway in the Mouse**
Enzo Lalli, Valbonne

11:55 **Topic C: In vitro Models**
William E. Rainey, Augusta, USA

12:15 **Topic D: Regulation of the Late Pathway of Aldosterone Biosynthesis**
Celso E. Gomez-Sanchez, Jackson, USA

12:35 **Topic E: Potassium Channels in APA**
Richard Warth, Regensburg

12:45 *Lunch*

13:30 **Session III Breaking News in PA: Free Communications from all fields of PA (5' presentation and 3' discussion)**
Chairs: L. C. Rump, Francesco Fallo

15:15 *Coffee Break*

Session IV Adrenal Vein Sampling: A Gold Standard?
Chairs: F. Mantero, J. Funder

15:45 **Topic A: The Mayo Clinic Experience**
William Young, Mayo Clinic, Rochester, USA

16:05 **Topic B: The real Word in Germany**
Oliver Vonend, Düsseldorf

16:25 **Topic C: Rapid Cortisol Measurement**
Martin Bidlingmaier, Munich

16:45 **Topic D: Does AVS predict Outcome?**
Jacques Lenders, Nijmegen

17:05 **Topic E: AVS around the World**
Gian-Paolo Rossi, Padua

17:25 **Topic F: Perspectives for a Guideline**
Bruno Allolio, Würzburg

19:00 **Dinner in the Schlosscafé im Palmenhaus**

Friday, May 6th 2011

Session V Screening and Diagnosing PA: What is new?

Chairs: H. Wallaschofski, L. Sechi

09:00 **Topic A: Prevalence of PA in Population-based Studies**
Anke Hannemann, Greifswald

09:20 **Topic B: Conditions affecting the ARR**
Michael Stowasser, Brisbane, Australia

09:40 **Topic C: Who should be screened for PA?**
Paolo Mulatero, Torino

10:00 **Topic D: Role of Confirmatory Tests**
Franco Mantero, Padua

10:20 **Topic E: Predicting Surgical Success in PA**
Pierre-François Plouin, Paris

10:40 *Coffee Break*

Session VI Aldosterone excess, Classical and Non classical Effects

Chairs: M. Stowasser, M. Reincke

11:20 **Topic A: PA and the Metabolic Syndrome**
Francesco Fallo, Padua

11:40 **Topic B: Aldosterone and the Kidney**
Marcus Quinkler, Berlin

12:00 **Topic C: Anxiety and Depression in PA**
Heike Künzel, Munich

12:20 **Topic D: Aldosterone and the Heart**
Leonardo Sechi, Udine

12:40 **Topic E: PA and Vessels**
Jiri Widimsky, Prague

13:00 **Closing Remarks and Farewell**
Martin Reincke, Munich

13:15 *Lunch*

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Progress in Primary Aldosteronism 2

From basic research to clinical evidence

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Progress in Primary Aldosteronism 2

From basic research to clinical evidence

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Abstracts

Free Communications and Breaking News in PA

1. Tomaschitz A. et al.: Genome-wide Association Study Identifies Genetic Variations influencing ARR levels in Caucasian: the Ludwigshafen Risk and Cardiovascular Health (LURIC) Study.
2. Willenberg H. et al.: The saline infusion test produces lower cut-off values than the fludrocortisone suppression test.
3. Tizzani D. et al.: Concurrent Primary Aldosteronism and Subclinical Cortisol Hypersecretion. A Perspective Study.
4. Ronconi V. et al.: Progesterone increase counteracts aldosterone action in a pregnant woman with primary aldosteronism.
5. Maniero C. et al.: Subtle hyperparathyroidism: a novel feature of primary aldosteronism that is corrected by adrenalectomy.
6. Salcuni A. et al.: BMD and primary hyperaldosteronism: a pilot study.
7. Giacchetti G. et al.: Primary aldosteronism and essential hypertension: assessment of the global cardiovascular risk at diagnosis and follow-up.
8. Somloova Z. et al.: Are there metabolic differences in two main types of primary aldosteronism?
9. Fischer E. et al.: Effect of adrenal vein sampling based decision making on adrenalectomy rate and clinical outcome in patients with primary aldosteronism.
10. Barisa M. et al.: Use and interpretation of adrenal vein sampling for differentiating the major subtypes of primary aldosteronism: results of the Adrenal Vein Sampling International Study (AVIS).

GENOME-WIDE ASSOCIATION STUDY IDENTIFIES GENETIC VARIATIONS INFLUENCING ARR LEVELS IN CAUCASIAN: THE LUDWIGSHAFEN RISK AND CARDIOVASCULAR HEALTH (LURIC) STUDY.

Andreas Tomaschitz[1], Stefan Pilz[1,2], Eberhard Ritz[3], Marcus E Kleber[4,5], PhD, Bernd Genser[4], Tanja Grammer[4], Michael M Hoffmann[6], Bernhard O. Boehm[7], Bernhard R Winkelmann[8], Winfried März[4,9,10]

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[5]LURIC Study nonprofit LLC, Freiburg, Germany
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INTRODUCTION

Inadequately high and autonomous adrenal aldosterone secretion in regard to its principal trophin renin is reflected by an elevated aldosterone to renin ratio (ARR) levels. An increased ARR is related to higher blood pressure levels, pointing to a potential role of inappropriately elevated aldosterone levels in mediating the development of arterial hypertension and cardiovascular disease.

To identify common genetic polymorphisms associated in the pathogenic pathway of an elevated ARR in individuals of European ancestry, we performed a genome-wide association study (GWAS) in 3300 Caucasians referred to coronary angiography.

METHODS

We performed a genome-wide association study (GWAS) in about 3300 Caucasians referred to coronary angiography using samples genotyped with the Affymetrix Genome-Wide Human SNP array 6.0 as well as the Affymetrix Human Mapping 500k. Samples were imputed to HapMap2 using MACH. After removing SNPs with a probability < 0.9, call rate < 0.95, hardy Weinberg equilibrium < 10^{-4} and minor allele frequency < 0.01 the data sets comprised 3,702,211 SNPs and 1,545,540 SNPs, respectively. GWAS was done assuming an additive model using the software GoldenHelix. Results have been analyzed using the software WGAViewer.

One genomic region with one or more sequence variants was associated with ARR values ($p < 1 \times 10^{-7}$) and five genomic regions were related to ARR values ($p < 1 \times 10^{-6}$), **Table 1**.

RESULTS

One single-nucleotide polymorphisms located on chromosome 11 (11p11.2) achieved genome-wide significance with ARR levels [$P=9.41\times10^{-7}$]. The top SNP associated with mean ARR values was rs11039480 (gene: PTPRJ (protein tyrosine phosphatase, receptor type) [**Figure 1.** Manhattan plot presenting all SNP *P* values organized by chromosome and genomic position]. PTPRJ is of interest, as it encodes a group of enzymes that are involved in many cellular functions such as protein interactions processes, protein stability, cell growth, differentiation, proliferation and regulation of enzyme activity. In particular protein thyrosine phosphatase activity is a key factor in the regulation in signal transduction pathways such as the mitogen-activated protein (MAP) kinase pathway, which has been shown to mediate adrenal aldosterone secretion by increasing sensitization of adrenocortical cells to angiotensin II.

Other top associations in our GWAS are summarized in **Table 1**.

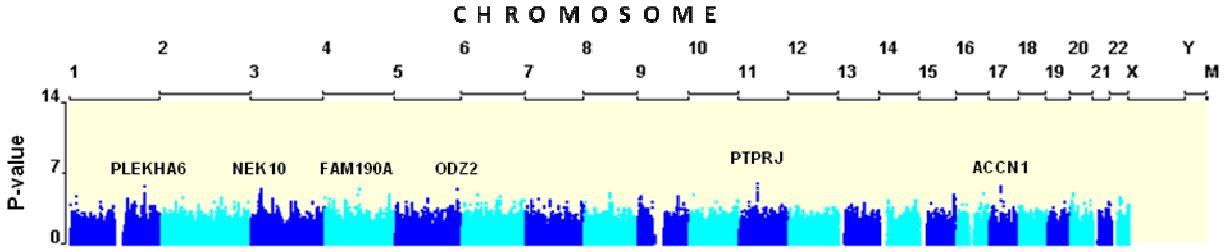
CONCLUSIONS

We identified one SNP reaching genome-wide significance for ARR levels in or near the gene PTPRJ. Our results therefore suggest the relevance of the protein tyrosine phosphorylation in susceptibility for varying ARR levels. These findings may further provide new insight into the pathogenesis of diseases related to inappropriately elevated aldosterone levels. Although these findings require replication and further study, our findings provide novel evidence that specific genetic predispositions might underline increased adrenal aldosterone production independent of its principal trophin renin.

Table 1. SNPs associated with the aldosterone to renin ratio at a significance level of P x 10^{-7} to 10^{-6}

SNP	Nearest gene	Location	Discovery P
rs11039480	PTPRJ protein tyrosine phosphatase, receptor type	Chromosome 11: 48,002,110-48,192,393 forward strand.	9.41 x 10^{-7}
rs9901562	ACCN1, amiloride-sensitive cation channel 1, neuronal	Chromosome 17: 31,340,105-32,483,551 reverse strand.	1.96 x 10^{-6}
rs35457431	PLEKHA6, pleckstrin homology domain containing, family A member 6	Chromosome 1: 204,190,349-204,329,044 reverse strand.	2.07 x 10^{-6}
rs1363203	ODZ2, odz, odd Oz/ten-m homolog 2 (Drosophila)	Chromosome 5: 166,711,804-167,691,162 forward strand.	3.25 x 10^{-6}
rs17017223	FAM190A, family with sequence similarity 190, member A	Chromosome 4: 91,048,686-92,523,064 forward strand.	4.30 x 10^{-6}
rs513646	NEK10, NIMA (never in mitosis gene a)- related kinase 10	Chromosome 3: 27,151,576-27,410,951 reverse strand.	4.33 x 10^{-6}

Figure 1. Manhattan plot of genome wide association analyses. *P* values of the additive genetic model for each SNP associated with the aldosterone to renin ratio in European-ancestry participants are shown.



THE SALINE INFUSION TEST PRODUCES LOWER CUT OFF VALUES THAN THE FLUDROCORTISONE SUPPRESSION TEST.

Melania Balaş [1,2], Holger S. Willenberg [2]

[1] Department of Endocrinology, Diabetes and Rheumatology, University Hospital Duesseldorf, Germany;
[2] Department of Endocrinology, University of Medicine and Pharmacy "Victor Babeş"; Timişoara, Romania

Background/Objective: The clinical practice guideline on primary aldosteronism (PA) published recently by the Endocrine Society suggests to use a lower cut-off value for confirmation in the fludrocortisone suppression test (FST) than in the saline infusion test (SIT). Here we studied patients with PA or essential hypertension who underwent one or the other test or both of them.
Results: Using the DPC Siemens aldosterone radioimmunoassay, we found that SIT led to a stronger suppression of aldosterone than the FST with approximately 90 percent accuracy ratios. Post test aldosterone to renin ratios (ARR) and the delta in aldosterone serum concentrations performed worse. The same results were observed in patients who underwent both FC and SIT.
Conculsion: For the SIT, a lower cutoff-value should be used than proposed in the guideline and for the FC. It seems that lower cut-off values are to be used for the adequate identification of patients with unilateral PA. We need long-term prospective studies for addressing the question at what cut-off values patients benefit from subtype differentiation of PA.

CONCURRENT PRIMARY ALDOSTERONISM AND SUBCLINICAL CORTISOL HYPERSECRETION. A PERSPECTIVE STUDY

D. Tizzani[1], C. Bertello[1], N. Sonino[3], A. Fassina[4], M.C. Zennaro[5], S. Boulkroun[5], S. Monticone[1], V. Crudo[1], J. Burrello[1], F. Veglio[1], F. Fallo[2], P. Mulatero[1].

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Background: Cortisol hypersecretion from an aldosterone-producing adenoma has been reported anecdotally. In the absence of overt Cushing's syndrome, the true prevalence of concurrent aldosterone and subclinical cortisol hypersecretion may be underestimated since hypercortisolism is not routinely investigated in primary aldosteronism. **Objective**: To perspectively estimate the occurrence of subclinical hypercortisolism in patients with primary aldosteronism. **Methods:** Within a large population of hypertensive patients studied over the last 2 years, 76 had primary aldosteronism and were further investigated. No patient had clinical signs of hypercortisolism. Differential diagnosis between unilateral and bilateral aldosterone hypersecretion was made by CT/MRI and/or by adrenal venous sampling (AVS) with aldosterone/cortisol ratio. Subclinical hypercortisolism was defined by failure to suppress plasma cortisol to <50 nmol/L after 1 mg-overnight dexamethasone (dex), initially used as screening test, and at least one of two abnormal tests, i.e. ACTH <2 pmol/L and urine cortisol >694 nmol/d. **Results:** Unilateral adrenal disease was found in in 34 patients (micronodular hyperplasia, n=2; adenoma, n=32)**.** Three out of these patients had pl. cortisol >50 nmol/L after dex. Only one (M, 71 y.o.) showed low-normal ACTH (1.7 pmol/L) and mildly elevated ur. cortisol (894 nmol/d) in addition to no suppression of pl. cortisol by dex (104 nmol/L). The patient had a right 4 cm adrenal mass at CT scan, and no AVS was performed. Laparoscopic adrenalectomy was followed by short-term steroid replacement to prevent adrenal insufficiency. All criteria for adrenocortical adenoma were fulfilled at histology, with a marked prevalence of *zona-fasciculata* like cells in the tumor. *In situ* hybridization showed expression of *CYP11B1* only in tumoral tissue and *CYP11B2* expression only in the peri-tumoral area, suggesting the co-existence of a cortisol-producing adenoma and an aldosterone-producing hyperplasia in the same adrenal. Restoration to normal of ACTH, ur. cortisol and pl. cortisol response to dex, as well as serum K^+ and aldosterone normalization, was seen at 6 months after surgery. **Conclusions:** Concurrent aldosterone and subclinical cortisol hypersecretion is a rare event in patients with primary aldosteronism. However, we suggest to perform an overnight dex suppression test in all these patients and, in case of a positive result, to proceed with further assessment of pituitary-adrenal function. In fact, concomitant subclinical hypercortisolism in PA patients may give misleading AVS results and, in case of surgery, implies a careful perioperative management.

PROGESTERONE INCREASE COUNTERACTS ALDOSTERONE ACTION IN A PREGNANT WOMAN WITH PRIMARY ALDOSTERONISM

Ronconi V., Turchi F., Zennaro M.-C.*, Appolloni G., Boscaro M, Giacchetti G.

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Pregnancies in patients with primary aldosteronism (PA) are often characterized by maternal and fetal complications, including end organ damage, placental abruption, pre-term delivery, intrauterine death and fetal distress. Blood pressure rarely decreases spontaneously. This report describes a case of a young woman followed up, after being diagnosed for primary aldosteronism due to bilateral adrenal hyperplasia, throughout her pregnancy, delivery and puerperium. Treatment with mineralocorticoid receptor antagonist was withdrawn during pregnancy because of the concern of causing possible feminization of male infant, and the patient was treated with calcium channel blocker and potassium supplementations, with good control of high blood pressure and maintenance of normokalemia. During pregnancy, despite progressive increase of aldosterone levels, blood pressure decreased to normal values so that she gradually discontinued antihypertensive treatment and continued only potassium supplementations. The course of pregnancy was uncomplicated; she had vaginal delivery at term (39 weeks of gestation) and gave birth to a healthy boy (Apgar score 1 and 5 min 10). The post delivery course was characterized by normotension until 4 days after delivery, then blood pressure began to rise again and she had to reintroduce antihypertensive treatment. After written informed consent was obtained, genetic analysis of mineralocorticoid receptor gene (NR3C2) was performed, but didn't show any mutation, while pathological examination of the placenta showed no signs of vascular damage.
A marked stimulation of aldosterone and plasma renin activity (PRA), up to five-to ten-fold by the end of pregnancy, is typical of normal pregnancy . Despite the striking expansion of blood volume, pregnant women usually remain normotensive due to the antagonising effect of progesterone on MR and peripheral vasorelaxation. In pregnant patients with PA aldosterone invariably increases while changes in PRA are not consistent. The mechanisms for worsening of hypertension or conversely for appearance of normotension are unknown. A possible explanation is that hypertension might persist or worsen when aldosterone levels exceed the normal pregnancy range so that progesterone is no longer able to antagonise its action. In this case, we observed the maintenance of normotension until 4 days after delivery, when progesterone decreased while aldosterone levels were still high. We therefore evaluated the progesterone/aldosterone ratio before and during pregnancy, and after delivery similarly to what had been previously reported in healthy pregnant women , with values for this ratio ranging from 18 to 80 (pmol $\cdot$ l^{-1}/pmol$\cdot$ l^{-1}) depending on the subject and on the week of gestation. In our patient hypertension reappeared when progesterone/aldosterone ratio fell below 20 (pmol $\cdot$ l^{-1}/pmol$\cdot$ l^{-1}), therefore we propose this cut-off value for a favourable pregnancy outcome. Finally, lack of dysregulation at the genetic level of MR and lack of evident vascular injury in the placenta of this patient, can be explained by adequate aldosterone effects counteracted by progesterone. Considering the high prevalence of PA among hypertensive patients, and the increasing number of patients diagnosed at young age, the occurrence of PA in pregnancy must be considered not as a rare condition but as a potentially common one that clinicians must be aware of.Further studies in pregnant women with PA of both subtypes will be necessary to evaluate the relevance of this ratio and to

define a cut-off value useful as prognostic tool for pregnancy outcome.
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SUBTLE HYPERPARATHYROIDISM: A NOVEL FEATURE OF PRIMARY ALDOSTERONISM THAT IS CORRECTED BY ADRENALECTOMY

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Objective: In vitro studies showed that PTH concentration-dependently increases aldosterone secretion from human adrenocortical cells; hence, hyperparathyroidism could be a mechanism driving aldosterone excess in PA.
Design and Method: To test this hypothesis we measured prospectively the plasma levels of intact (1-84)-PTH, total and ionized calcium, inorganic phosphorus, magnesium, potassium, PRA, aldosterone (PAC), 1,25(OH)2D, 25(OH)D and the 24-hour urinary excretion of deoxypyridinoline (U-DPD), calcium and phosphorus in 109 consecutive hypertensive patients. Of them 49 had PA (due to aldosterone producing adenoma (APA) by the *"four corner criteria"* in 40, and to idiopathic hyperaldosteronism (IHA) in 9); 60 had primary hypertension (PH). These indexes were measured again after adrenalectomy in APA patients. We also sought for the PTH receptor expression in APA tissue by immunohistochemistry and RT-PCR.
Results: As compared to PH, the PA patients showed lower potassium, higher PAC, ARR, and PTH (APA 114±66 vs PH 79±32 ng/L; P=0.001). 25(OH)D showed similarly deficient levels in both PA and PH; no between-group differences were found for all other biochemical indexes of calcium and phosphorus metabolism. At follow-up post-adrenalectomy, besides the normalization of PAC, ARR, and potassium, a significant reduction of PTH (from 115±50 to 80±39 ng/L, p=0.01) with an increase of ionized calcium levels (from 1.16±0.04to1.21±0.03 mmol/L, p<0.05) was seen. Moreover, a significantly higher slope of the relation between PTH and ionized calcium was seen in PA than in PH patients. RT-PCR and immunohistochemistry showed the transcript and protein of the type 1 PTH receptor in APA.
Conclusions: Mild hyperparathyroidism can contribute to maintaining hyperaldosteronism acting on type 1 PTH receptor in APA despite suppression of the renin-angiotensin system. The higher slope of the relation between PTH and calcium in PA than in PH patients points to an alteration in calcium sensor as a mechanism of the subtle hyperparathyroidism in primary aldosteronism.

BMD AND PRIMARY HYPERALDOSTERONISM: A PILOT STUDY.

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Introduction

In rats with hyperaldosteronism, a reduction of bone mineral density (BMD) and cortical bone strength has been reported. The administration of spironolactone in men with congestive heart failure, has been associated with a reduction of risk fracture. The aim of this study is to evaluate BMD in patients with primary hyperaldosteronism (PA).

Subjects and Methods

Among the one-hundred twenty-three consecutive subjects with adrenal incidentaloma recruited between November 2009 and December 2010 in two referral Italian centers, sixty-seven hypertensive patients were screened for PA. In all patients, after an adequate pharmacological wash-out, the screening test with aldosterone-to-renin ratio (ARR) was performed. Fifteen subjects, showing ARR > 30 together with plasmatic aldosterone concentration (PAC) in upright position > 15 ng/dl, were suspected to have PA and underwent to a confirmatory test with saline infusion.

Six pts had PAC > 10 ng/dl and were considered affected by PA (group 1), 6 pts had PAC < 5 ng/dl and were considered not affected with PA (group 2). The remaining 3 pts had PAC between 5 and 10 ng/dl and have been excluded from this study. No patient was assuming drugs or was affecting with diseases that influences bone metabolism.

BMD (expressed as Z-value) at lumbar spine (LS) and femoral neck by dual X-ray absorptiometry (Hologic Discovery QDR series) and conventional spinal radiographs in lateral (T4-L4) and anteroposterior (AP) projection (L1–L4) were obtained in all subjects.

Results

Patients with PA (group 1, n = 6) as compared to patients without PA (group 2, n = 6), had a significantly lower BMD at LS (group 1: -1.55 ± 0.86, group 2: 0.74 ± 0.99; p = 0.006), Femoral Neck (group 1: -1.35 ± 0.58, group 2: 0.52 ± 1.17; p = 0.012) and Total Neck (group 1: -0.82 ± 0.54, group 2: 1.44 ± 1.27; p = 0.010). These data were confirmed after correction for BMI. There was 1 patients with vertebral fracture in each group.

Conclusions

This pilot study suggests that primary hyperaldosteronism is associated with low BMD both at LS and femoral neck.

PRIMARY ALDOSTERONISM AND ESSENTIAL HYPERTENSION: ASSESSMENT OF THE GLOBAL CARDIOVASCULAR RISK AT DIAGNOSIS AND FOLLOW-UP

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High blood pressure represents the first cause of mortality in the general population worldwide.
Aim of the study was to evaluate the cardiovascular risk according to the ESH/ESC 2007 guidelines for the treatment of hypertension, in patients with primary aldosteronism (PA) and with essential hypertension (EH), at diagnosis and at follow-up. We studied 71 PA patients (29 with aldosterone producing adenoma-APA and 42 with idiopathic hyperaldosteronism-IHA, M/F 42/29, mean age 51$\pm$12 yr, BMI 27$\pm$ 4 Kg/m^2) and 80 essential hypertensives (M/F 23/57, mean age 55$\pm$11 yr, BMI 31$\pm$ 7 Kg/m^2), at basal and after surgical or medical treatment. After a mean follow-up period of 2.4 years for APA patients who underwent adrenalectomy, and 5.4 years for medically treated IHA, and 4 years for EH, patients were re-evaluated to assess the cardiovascular (CV) risk.
The resolution of hypertension was observed in 48% of APA and 35% of IHA.
According to the ESH/ESC 2007 guidelines the CV risk in PA was, respectively at diagnosis and follow-up: low in 0% and 7%, moderate in 11% and 25%, high in 55% and 47%, very-high in 34% and 21%. Moreover, while 26% of patients had a grade 3 hypertension at diagnosis, only 1% had the same grade at follow-up.
The reduction of global CV risk was more evident in APA patients than in IHA, in whom, anyway, a significant increase of HDL cholesterol was observed, together with a reduction of left ventricular cardiac mass and posterior wall thickness ($p<0.05$). Considering the prevalence of the very high risk category, a marked reduction after treatment was observed in APA (41% vs 17%), while the reduction was less evident in IHA (30% vs 25%) and very modest in EH (16% vs 14%).
As for EH, the CV risk was at diagnosis and follow-up, respectively: low 3% vs 12%, moderate 15% vs 25%, high 66% vs 49%, very high 16% vs 14% ($p<0.05$).
Despite the same distribution of severity of hypertension among the three groups, the global CV risk was higher in PA than in EH patients, highlighting the deleterious effects of aldosterone excess on CV risk beyond blood pressure.
In conclusion, patients with PA present a high CV risk, which is however in great part reversible after specific treatment, due both to the reduced blood pressure values and to the improvement of end-organ damage. EH patients display a less evident reduction of the CV risk after treatment due to less consistent reduction of blood pressure and to the small improvement of cardiovascular risk factors.

ARE THERE METABOLIC DIFFERENCES IN TWO MAIN TYPES OF PRIMARY ALDOSTERONISM?

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Metabolic syndrome is frequent clinical condition in the population of hypertensive subjects. Primary aldosteronism (PA) is common form of secondary hypertension. This study was aimed at investigating the prevalence of the metabolic syndrome and its components in two main forms of PA: unilateral aldosterone-producing adenoma (APA) and bilateral aldosterone overproduction due to idiopathic hyperaldosteronism (IHA). The distinction between both types of PA was based on adrenal venous sampling and/or successful surgery with histopathological examination. We analyzed clinical and laboratory data in 100 patients with PA (50 patients with IHA and 50 patients with APA) and 90 patients with essential hypertension (EH). We compared clinical and laboratory parameters between all groups of patients. The prevalence of the metabolic syndrome (62 vs. 36%), the body mass index value (30 ± 4 vs. 27± 5) and triglycerides levels (1, 9 ± 0, 9 vs. 1, 4± 0, 8 mmol/l) were all significantly (p < 0, 05) higher in IHA compared to APA patients. Our data thus indicate potential differences in metabolic phenotype between two main forms of PA. Metabolic profile of patients with bilateral form of PA (due to IHA) is similar to EH in contrast to unilateral form of PA (APA). According to our study it looks like that the prevalence of IHA is higher in males than in females.

EFFECT OF ADRENAL VEIN SAMPLING BASED DECISION MAKING ON ADRENALECTOMY RATE AND CLINICAL OUTCOME IN PATIENTS WITH PRIMARY ALDOSTERONISM

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Context Adrenal vein sampling (AVS) is endorsed by the Endocrine Society Practice Guidelines in the differential diagnosis of unilateral aldosterone producing adenoma (APA) from idiopathic bilateral adrenal hyperplasia (IAH). CT and MRI appear to have a low accuracy for APA. Whether treatment decisions based on AVS result in a more favorable clinical outcome is controversial.
Objective We compared the rate of adrenalectomy and its consecutive clinical outcome in patients with primary aldosteronism (PAL) having AVS based treatment decision versus imaging based treatment decisions.
Design, Setting, and Patients We retrospectively studied 66 of 138 patients of the Munich PAL registry who had been adrenalectomized because of suspected APA. Patients were stratified into groups according to AVS based or imaging based decision making: 35 patients underwent adrenalectomy following technically successful AVS (group 1), 15 following non-successful AVS (group 2), and 16 patients did not undergo AVS (group 3). The clinical outcome parameters were assessed prospectively.
Main outcome measures Rate of adrenalectomy related to total number of patients, remission from PAL.
Results Patients undergoing AVS were more likely to have adrenalectomy (group 1: 67%; group 2: 60% versus 42% in group 3; $p<0.05$). Remission and improvement rates of hypertension were not significantly different between groups.
Conclusion Our single center study suggests that performing AVS in patients with PAL increases the percentage of patients eligible for adrenalectomy.

USE AND INTERPRETATION OF ADRENAL VEIN SAMPLING FOR DIFFERENTIATING THE MAJOR SUBTYPES OF PRIMARY ALDOSTERONISM: RESULTS OF THE ADRENAL VEIN SAMPLING INTERNATIONAL STUDY (AVIS).

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Background. The main causes of primary aldosteronism are bilateral adrenal hyperplasia (BAH) and aldosterone-producing adenoma (APA), which feature non-lateralised and lateralised aldosterone excess, respectively. The differentiation between these causes is crucial for the choice of medical or surgical treatment of PA and requires adrenal venous sampling (AVS).

Progress in Primary Aldosteronism 2

Deutsches Conn-Register
Else Kröner-Fresenius Conn-Register

From basic research to clinical evidence

Objective. Since use and interpretation of AVS remains challenging because of the lack of accepted criteria, we performed a large international multicenter study involving referral centres to determine a) how AVS is being performed and interpreted; b) what its rate of major complications is.
Design and method. The centres were identified through a literature search and invited to participate to the AVIS Study, which entails 2 phases. In the first phase, which was concluded in November 2010, data on rate of use of AVS in PA patients, modalities of performance and interpretation of the test, and rate of adrenal vein rupture were analysed. In the second phase, which is ongoing, data on individual AVS studies will be gathered.
Results. Nineteen of the 23 (82.6%) centres that were initially invited agreed to participate. They are scattered all over Asia, Europe, North America and Australia. They furnished data on a total of 2595 AVS studies performed over the last 5 years. The percentage of PA patients systematically submitted to AVS resulted to be quite variable across these centres, ranging from 40% to 100% (median 77.5). The sequential catheterization technique was used at 63.2% of the centres while 36.8% use the bilaterally simultaneous technique. AVS was performed with ACTH stimulation at 52.6% of the centres. Analysis of the cut-off values used for assessing the selectivity, lateralization and contralateral suppression index showed a wide variability across centres. Moreover, some centres used absolute hormonal values, instead of established indexes for the diagnosis. Overall, the major complication rate was only 0.57%; it showed a significant heterogeneity across centres with most complications being accounted for by only few centres. A significant correlation between complication rate and number of radiologists performing AVS at each center was found ($r= 0.543$; $p<0.05$).
Conclusions. This large survey on AVS, showed that: 1) AVS is being performed at a very low complication rate at most referral centres worldwide; 2) most centres continue to use ACTH stimulation even though this was shown to confound the assessment of lateralization; 3) notwithstanding the lack of any theoretical basis some centres continue to use absolute hormonal values instead of the appropriate indexes. Hence, these results emphasize the need for a consensus conference in order to optimize the clinical use of AVS.