# Prevalence of Primary Hyperaldosteronism in a Systemic Arterial Hypertension League

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## Summary

**Background: Until recently, primary hyperaldosteronism was considered a rare cause of secondary hypertension. However, in recent years, many studies have suggested that this disease can affect up to 20% of hypertensive individuals.**

**Objective: To determine the prevalence of primary hyperaldosteronism in hypertensive patients treated at the hypertension league of a university hospital.**

**Methods: Serum aldosterone and plasma renin activity levels were measured in 105 patients while they were undergoing standard antihypertensive treatment, with the exception of those using betablockers and spironolactone, in fasting condition and after rest in the supine position for 20 minutes. Those with an aldosterone/plasma renin activity ratio > 25 were submitted to the saline suppression test and, after the confirmation of the autonomy of aldosterone secretion, a computed tomography of the adrenals was performed. The results are presented as percentages and means and standard deviations.**

**Results: Of the 105 patients, 6.54% presented refractory hypertension. Nine presented an aldosterone/plasma renin activity ratio > 25 (8.5% of the total). Of these, 08 were submitted to the saline suppression test and 01 (with refractory hypertension) had the diagnosis of primary hyperaldosteronism confirmed (0.96% of the total). A computed tomography of the adrenals was performed, which showed normal results.**

**Conclusion: The prevalence of primary hyperaldosteronism in the studied sample was 0.96% of the total. However, when only the patients with refractory hypertension were evaluated, the prevalence was 14.3%. (Arq Bras Cardiol 2009;92(1):37-43)**

**Key words: Hyperaldosteronism; prevalence; hypertension.**

## Introduction

Primary hyperaldosteronism (PHA) is characterized by the increase in the levels of plasma and urinary aldosterone, suppression of the plasma renin activity (PRA), systemic arterial hypertension, hypokalemia and metabolic alkalosis[1].

The prevalence estimates of PHA that used hypokalemia as the diagnostic criterion varied from 0.05% to 2% of the population of hypertensive individuals[2]. However, from 1990 on, when several Centers started to adopt the aldosterone/PRA ratio in the triage of PHA, its prevalence increased to values > 12%[3].

It is admitted that this new strategy, correctly applied to the population of hypertensive individuals, can identify at least one among 10 individuals as having PHA[4].

Considering the estimate that there will be an increase in the prevalence of systemic arterial hypertension (SAH) of around 60% until 2025, which means that 30% of the world's population will be hypertensive[5], determining the prevalence of PHA, a cause of SAH that can be clinically treated with a specific therapy, directed by physiopathological mechanisms and even a curative one, becomes essential to decrease the complications caused by this disease.

Thus, the present study was designed to determine the prevalence of PHA in hypertensive patients undergoing treatment at the hypertension league of a university hospital.

## Methods

The study was carried out at the hypertension league of a university hospital. The EPINFO software was used to calculate the sample, based on the population of around 1,000 patients; considering a prevalence of 5% and a precision of 4%, we arrived at an n of 88, which was increased to 105 when estimating the losses of around 20%.

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The patients were selected by convenience, as they came for the consultations, from January to October 2007, following the exclusion criteria of the study, which were: use of betablocker, spironolactone, corticosteroids and oral contraceptives, as well as pregnancy.

The selected patients answered a questionnaire, through which their demographic characteristics and symptomatology were evaluated. All patients were submitted to a physical examination that included blood pressure measurements in both upper limbs, with patients in the sitting position.

All patients underwent laboratory assessment that measured serum sodium and potassium, creatinine, serum aldosterone and plasma renin activity and the aldosterone/PRA ratio was calculated.

Blood collection for aldosterone and PRA measurement was carried out in the morning under fasting condition and after 20 minutes of rest in the supine position, without anti-hypertensive medication withdrawal and under routine diet.

The blood for PRA measurement was stored in pre-refrigerated tubes containing Ethylene-diamine-tetra-acetic Acid (EDTA) and the plasma was separated immediately after the collection in a centrifuge refrigerated at 4º Celsius. The PRA measurement was carried out by the in vitro generation of angiotensin I by radioimmunoassay, using a commercially available kit, Renin Maia™ (Adaltis Italia, Italy). The intra-assay and interassay coefficients of variation were 3.39 - 5.1% and 3.82 - 5.15%, respectively, and the normality values for PRA in the supine position ranged from 0.51 - 2.64 ng/mL/h.

The blood for aldosterone measurement was stored in plastic tubes and the serum was separated immediately after collection in a common centrifuge. Serum aldosterone was measured with the use of a solid-phase radioimmunoassay based on specific aldosterone antibodies immobilized on the wall of a propylene tube (Coat-A-Count Aldosterone, PITKAL™ - 4, Los Angeles, USA). The intra- and interassay coefficients of variation were 2.3 - 5.4% and 3.8 - 15.7%, respectively, with the normality values for aldosterone in the supine position ranging from 1 - 16 ng/dL.

The blood samples for PRA and aldosterone measurement were stored in a freezer at - 20º Celsius for a period of one to two weeks until they were sent to the central lab (Hermes Pardini Laboratory, Belo Horizonte, MG).

The samples were sent in 5-liter Styrofoam boxes containing recyclable ice, in order to maintain the adequate temperature throughout delivery. The transportation was carried out by plane, totaling six hours until the final destiny.

The aldosterone/PRA ratio was obtained through the division of the serum aldosterone value (ng/dL) by the simultaneous PRA value (ng/mL/h) and a value > 25 was defined as a positive triage test for PHA.

The patients that presented an aldosterone/PRA ratio > 25 underwent the suppression test, with the infusion of 2 liters of saline solution at 0.9% IV for 4 hours (8AM-12PM) and serum aldosterone measurements before and after the saline overload. The presence of serum aldosterone > 05 ng/dL after the infusion of the saline solution confirmed the autonomy of the aldosterone secretion, and consequently, the diagnosis of PHA.

The following step was to determine the etiology of the PHA. A computed tomography of the adrenals was carried out with 03 mm slices, before and after the administration of iodated contrast, in the patient in whom the autonomy of aldosterone secretion was confirmed.

The presence of a single unilateral adrenal macroadenoma with a contralateral normal adrenal was the criterion adopted to diagnose an aldosterone-producing adenoma (APA).

The combination of the hormonal and biochemical criteria described above with the CT of the adrenals showing bilateral micronodular hyperplasia or apparently normal glands, was considered a diagnostic criterion of bilateral adrenocortical hyperplasia (BAH).

The data were organized and analyzed with the EPINFO software. The quantitative variables are presented as means and standard deviations, whereas the qualitative variables were presented as percentages.

The research was approved by the Ethics Committee in Research of the University Hospital and a Free and Informed Consent Form was signed by all patients.

## Results

From January to October 2007, 107 patients were included in the research protocol of primary hyperaldosteronism (PHA), of which 105 underwent the triage tests that were necessary for the diagnosis.

Of the 105 patients, 7 (6.54%) presented refractory arterial hypertension. The demographic characteristics of the sample are shown in Table 1.

**Table 1 - Demographic characteristics of the 105 hypertensive patients included in the research protocol of primary hyperaldosteronism, from January to October 2007, at *Hospital Universitário da Universidade Federal do Maranhão***

| | |
|---|---|
| Female sex (%) | 75.2 |
| Male sex (%) | 24.8 |
| Age (yrs) | 55.1 ± 11.2 |
| HR (bpm) | 74.4 ± 9.5 |
| SAP (mmHg) | 138.1 ± 20.1 |
| DAP (mmHg) | 83.4 ± 11.7 |
| Optimal, normal and borderline BP (%) | 54.8 |
| SAH Stage I (%) | 34.6 |
| SAH Stage II (%) | 7.7 |
| SAH Stage III (%) | 2.9 |
| Refractory SAH (%) | 6.54 |
| Number of Antihypertensive drugs used | |
| 1(%) | 26.17 |
| 2 (%) | 58.88 |
| 3 (%) | 12.15 |
| 4 (%) | 2.80 |

*HR - heart rate; SAP - systolic arterial pressure; DAP - diastolic arterial pressure; BP – blood pressure; SAH - systemic arterial hypertension.*

All patients were receiving antihypertensive therapy and the medication frequency can be seen in Table 2.

The biochemical parameters of the patients included in the research protocol can be seen in Table 3. Of the 105 study patients, nine (8.5%) presented serum potassium < 3.5 mg/dL and another nine (8.5%) presented an aldosterone/PRA ratio > 25(ng/dL)/(ng/mL/h); no association was observed between these two parameters, as shown in Table 4. Table 5 shows the serum aldosterone values and PRA values of the 9 patients with an aldosterone/PRA ratio > 25.

The suppression test with saline solution infusion was carried out to confirm PHA in 8 of the 9 patients with a positive initial triage test. Of these, only one patient, with refractory arterial hypertension, had the diagnosis of PHA confirmed (0.96% of the total sample). The other 7 patients presented aldosterone suppression, confirming the presence of essential SAH. These results can be seen in Table 6.

A CT of the adrenals was carried out with 3-mm thick slices in the patient with a confirmed syndromic diagnosis of PHA, which was considered normal, as shown in Figure 1.

Once the autonomous secretion of aldosterone was confirmed, and consequently, the diagnosis of PHA, the

**Table 2 - Antihypertensive drugs being used by the 105 hypertensive patients included in the research protocol of primary hyperaldosteronism, from January to October 2007, at *Hospital Universitário da Universidade Federal do Maranhão***

| Antihypertensive drugs | % |
|---|---|
| ACEI | 78.5 |
| Thiazide diuretics | 69.0 |
| Calcium channel blockers | 23.3 |
| Angiotensin II Receptor Blockers | 9.3 |

*ACEI - Angiotensin-converting enzyme inhibitors.*

**Table 3 - Biochemical parameters of the 105 hypertensive patients included in the research protocol of primary hyperaldosteronism, from January to October 2007, at *Hospital Universitário da Universidade Federal do Maranhão***

| Variable | Mean ± SD |
|---|---|
| Serum creatinine (mg/dL) | 0.8 ± 0.2 |
| Serum potassium (mg/dL) | 4.1 ± 0.4 |
| Serum sodium (mg/dL) | 141 ± 2.9 |
| Serum aldosterone (ng/dL) | 5.1 ± 4.1 |
| Plasma Renin Activity (ng/mL/h) | 1.8 ± 2.0 |
| Aldosterone/PRA ratio (ng/dL) / (ng/mL/h) | 8.1 ± 11.9 |

*SD - standard deviation; PRA - plasma renin activity.*

**Table 4 - Association between serum potassium and aldosterone/plasma renin activity ratio > 25 in the hypertensive patients included in the research protocol of primary hyperaldosteronism, from January to October 2007, at *Hospital Universitário da Universidade Federal do Maranhão***

| Patient | Serum K+ (mg/dL) | Aldosterone/PRA ratio (ng/dL) / (ng/mL/h) |
|---|---|---|
| 1 | 3.9 | 52 |
| 2 | 4.3 | 67 |
| 3 | 4.2 | 34.5 |
| 4 | 3.5 | 49 |
| 5 | 4.2 | 27.5 |
| 6 | 4.0 | 42.8 |
| 7 | 3.8 | 25 |
| 8 | 4.1 | 26.6 |
| 9 | 4.1 | 39.5 |

*K+ - potassium; PRA - plasma renin activity.*

**Table 5 - Serum aldosterone and plasma renin activity levels in the 9 hypertensive patients from the research protocol of primary hyperaldosteronism that presented aldosterone/plasma renin activity ratio > 25 (January to October 2007, at *Hospital Universitário da Universidade Federal do Maranhão*)**

| Patient | Serum aldosterone (ng/dL) | PRA (ng/mL/h) | Aldosterone/PRA ratio (ng/dL) / (ng/mL/h) |
|---|---|---|---|
| 1 | 5.2 | 0.1 | 52 |
| 2 | 6.7 | 0.1 | 67 |
| 3 | 6.9 | 0.2 | 34.5 |
| 4 | 4.9 | 0.1 | 49 |
| 5 | 5.5 | 0.2 | 27.5 |
| 6 | 21.4 | 0.5 | 42.8 |
| 7 | 7.5 | 0.3 | 25 |
| 8 | 8.0 | 0.3 | 26.6 |
| 9 | 7.9 | 0.2 | 39.5 |

*PRA - plasma renin activity.*

**Table 6 - Outcome of the saline suppression test in the 8 patients from the research protocol of primary hyperaldosteronism that presented aldosterone /plasma renin activity ratio > 25 (January to October 2007, at *Hospital Universitário da Universidade Federal do Maranhão*)**

| Patient | Pre-Infusion Aldosterone (ng/dL) | Post-Infusion Aldosterone (ng/dL) |
|---|---|---|
| 1 | 8.0 | 2.1 |
| 2 | 6.8 | 0.5 |
| 3 | 8.2 | 1.7 |
| 4 | 13.1 | 6.6 |
| 5 | 11.6 | 1.7 |
| 6 | 7.0 | 3.0 |
| 7 | 7.4 | 2.5 |
| 8 | 9.9 | 2.8 |

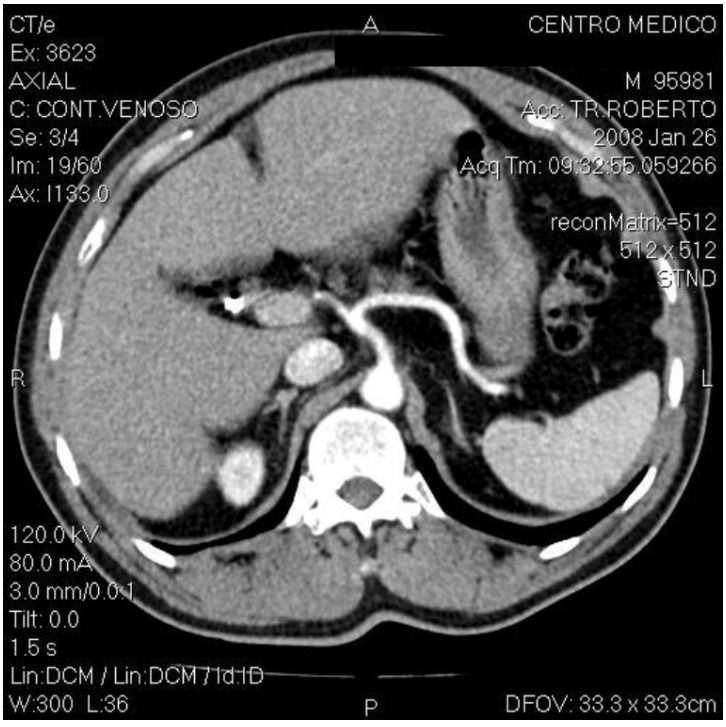


*Figure 1 - Computed tomography of the adrenal glands of patient with a diagnosis of primary hyperaldosteronism.*

patient's treatment was started with spironolactone (25 mg/day).

## Discussion

The present study used the aldosterone/PRA ratio of 105 patients to investigate the presence of PHA and found a prevalence of 0.96% of the total sample. However, when only the patients with refractory arterial hypertension are considered, the prevalence of PHA increased to 14.3%.

Although several studies have demonstrated a significant increase in the PHA prevalence with the use of the aldosterone/PRA ratio, there is no scientific consensus about this epidemic, especially considering the lack of standardization of the triage test[6].

The aldosterone/PRA ratio is influenced by posture, diet and can vary from high to normal in repeated studies of the same individual[6].

In the present study, blood collection for aldosterone and PRA measurement was carried out in the morning under fasting condition and after 20 minutes of rest in the supine position, without anti-hypertensive medication withdrawal. The cutoff of the aldosterone/PRA ratio > 25 was adopted as positive for the PHA triage.

Currently, the aldosterone/PRA ratio > 25 has been used as the main assessment procedure in the investigation of PHA[1]. Giacchetti et al[7], using 25 as the cutoff for the aldosterone/PRA ratio obtained in the supine position, obtained a sensitivity of 98.3% and a specificity of 67%, with a positive and negative predictive value of 68% and 39%, respectively.

There was a predominance of the female sex in the studied sample, which reflects the situation observed in medical offices, where women are more present than men[8].

Age varied from 33 to 95 years, with a mean of 55.1 years, in accordance with what was described by other authors[8-11].

Of the 105 patients, 7 (6.54%) had refractory arterial hypertension, including the patient who had the diagnosis of PHA confirmed, which presented stage II SAH, in spite of the four different classes of anti-hypertensive drugs used (ACEI, thiazide diuretics, calcium channel blocker and sympatholytic with central action) and the fact that he had diabetes. This information is in accordance with the medical literature, where it is observed that PHA is more common among patients with refractory SAH[12].

Umpierrez et al[11], studying 100 diabetic and refractory hypertensive patients, found a prevalence of 14% of PHA in this population. All study patients were undergoing treatment with anti-hypertensive drugs, with 78.5% of them receiving ACEI and 69% receiving thiazide diuretics.

It is known that anti-hypertensive drugs are capable of interfering with the aldosterone/PRA ratio, especially due to its influence on PRA.

According to the study carried out by Mulatero et al[13] in 230 patients to evaluate the effect of anti-hypertensive drugs on the aldosterone/PRA ratio, the alpha-blockers and the ACEI do not significantly interfere in the diagnosis of PHA. As for amlodipine and betablockers, they increase the incidence of

false-negative and false-positive results, respectively.

The PRA tends to be lower in patients using betablockers, which increases the number of false-positive results and the need for confirmatory tests; therefore, patients using these medications were excluded from this study.

Nevertheless, Nishizaka et al[10], evaluating 265 refractory hypertensive patients with the objective of establishing the validity of the aldosterone/PRA ratio in Caucasian and Black individuals, found similar cutoff values of the aldosterone/PRA ratio for patients undergoing treatment with or without betablockers.

Even considering this knowledge, we have sought not to interfere with the patients' medication, supporting the actual perspective of a triage test[14,15].

Hypokalemia was not observed in the patient with PHA. This information is in accordance with most of the literature studies, in which hypokalemia has been found in a decreasing number of patients with PHA (up to 35% of the cases)[3,9].

Mosso et al[8], studying 100 hypertensive patients with BP > 145 x 95 mmHg, found a 10% prevalence of PHA and none of the patients presented hypokalemia. Rossi et al[16], in a study with 1,125 hypertensive patients, found a 4.8% prevalence of PHA, with hypokalemia present in 9.6% of the patients.

The mean of aldosterone of the studied sample was 5.1 ng/dL and the patient with a confirmed diagnosis of PHA presented serum aldosterone of 4.9 ng/dL at the triage assessment for the disease. These values are considered low when compared to the results of other literature studies. Umpierrez et al[11] (n = 100) found mean aldosterone values of 9.1 ± 6 ng/dL in essential hypertensive individuals and 15.6 ± 8 ng/dL in those with PHA. Loh et al[9] (n = 350), also described similar values, with a mean of 10.3 ± 0.4 ng/dL in normotensive individuals, 10.3 ± 0.4 ng/dL in essential hypertensive individuals and 21.9 ± 1.1 ng/dL in those with PHA[9]. Similar results were also described by Mosso et al[8] and Nishizaka et al[10]. Fogari et al[17], evaluating 3,000 non-selected hypertensive patients, obtained the following mean aldosterone values: 8.1 ± 3.8 ng/dL in essential hypertensive individuals and 13.6 ± 6.2 ng/dL in those with PHA.

Williams et al[18], in a study with 347 mildly hypertensive patients, presented similar results to that of the present study, with mean serum aldosterone values of 3.7 ± 0,2 ng/dL in normotensive individuals and 5.6 ± 0.2 ng/dL in hypertensive ones. Mean aldosterone levels of 11.4 ± 0.6 ng/dL were found among those with a positive triage test for PHA.

A possible explanation for the low values of aldosterone in the present study is the excessive sodium intake by the patients, as the results were similar to those obtained by Williams et al (n = 347), in which the individuals were on sodium-rich diet in order to undergo the triage test for PHA.

As for the PRA, the mean in the present study was 1.8 ng/mL/h, whereas the patient with a confirmed PHA diagnosis presented a mean PRA of 0.1 ng/mL/h. The general mean is considered high in comparison to other literature studies. Loh et al[9] (n = 350) reported means of 1.1 ± 0.10 ng/mL/h in the essential hypertensive individuals and 0.29 ± 0.09 ng/mL/h in those with PHA. Williams et al[18] (n = 347) described values of 0.6± 0.05 ng/mL/h in essential hypertensive individuals and 0.2 ± 0.02 ng/mL/h in those with a positive triage for PHA.

Nishizaka et al[10] (n = 265), evaluating the effect of anti-hypertensive drugs on the PRA, observed that it was higher among those patients using ACEI (4.1 ± 8.9 x 3.0 ± 6.2) and, especially, among those using thiazide diuretics (4.0 ± 8.5 x 1.6 ± 2.7), where the difference was statistically significant.

The fact that most of the study patients used ACEI in association with thiazide diuretics can justify the increase in PRA.

The mean of the aldosterone/PRA ratio in the present study was 8.1 (ng/dL)/(ng/mL/h), and the ratio in the patient with a confirmed PHA diagnosis was 49 (ng/dL)/(ng/mL/h). Loh et al[9] (n = 350) found a mean of 19.4 ± 1.2 (ng/dl)/(ng/ml/h) in the essential hypertensive individuals and of 484 ± 128.5 (ng/dl)/(ng/ml/h) in those with PHA. Williams et al[18] (n = 347) reported a mean of 14.8 ± 0.8 (ng/dl)/(ng/ml/h) in the essential hypertensive individuals and 64.8 ± 6 (ng/dl)/(ng/ml/h) in those with a positive triage for PHA.

In the present study, 9 patients (8.5% do total) presented an aldosterone/PRA ratio > 25 (ng/dl)/(ng/ml/h), of which 8 were submitted to the suppression test with saline solution IV to confirm the diagnosis of PHA and that was demonstrated in only one refractory hypertensive patient (0.96% of the total and 14.3% of the refractory hypertensive patients).

The seven patients with an aldosterone/PRA ratio > 25 (ng/dl)/(ng/ml/h) that had the serum aldosterone suppressed after the saline overload were considered to be patients presenting essential SAH with low renin.

The use of the aldosterone/PRA ratio has been the object of much criticism. For instance, low and even undetectable renin levels are common in elderly patients and long-term hypertensive individuals, increasing the aldosterone/PRA ratio, even in the presence of normal serum aldosterone levels.

Some Services such as the one in Torino (Italy), Rochester (Minnesota) and Singapore, adopt an aldosterone/PRA ratio associated to a minimum level of serum aldosterone for the triage of PHA, with the objective of decreasing the number of false-positive results[3]. Mulatero et al[19] consider an elevated aldosterone/PRA ratio in association with a serum aldosterone level > 15 ng/dL as the ideal triage method for the diagnosis of PHA. Passos et al[14] warn that the aldosterone/PRA ratio must be interpreted with caution when aldosterone levels are < 12 ng/dL. On the other hand, in Brisbane (Australia), there is no established cutoff for serum aldosterone, as well as in Santiago (Chile)[3,20]. The results are similar regarding the prevalence of PHA n all those Centers[3].

A study with 118 hypertensive and normokalemic patients carried out in the Mayo Clinic detected that 30% of them presented an increase in the aldosterone/PRA ratio, but only 13% of them had high aldosterone excretion as well[21].

In the present study, the cutoff > 25 was adopted as a positive triage test for PHA, regardless of the aldosterone values, prioritizing the higher sensitivity of the test.

According to the data of the Princess Alexandra Hospital, in Brisbane, only 19% of the patients that presented lateralization detected by the selective adrenal vein

catheterism had serum aldosterone levels > 15 ng/dL and many PHA diagnoses would be missed if the minimum serum aldosterone value were adopted as part of the triage test for the pathology[20].

In spite of the higher number of false-positive results when one eliminates the minimum serum aldosterone value from the PHA triage, they will be easily differentiated from true positive results through the suppression tests[11].

It is known that the aldosterone/PRA ratio alone is not enough to diagnose PHA. Less than 50% of the patients with a high aldosterone/PRA ratio fail to suppress the plasma or urinary aldosterone levels after an oral or IV saline overload[22].

Series from several authors have shown a high percentage of patients with an elevated aldosterone/PRA ratio, which, after the suppression test is performed, is reduced to values comparable to the prior PHA prevalence rates[6]. Therefore, the suppression tests are mandatory for the diagnosis of PHA[10].

In the present study, a suppression test was carried out with the IV infusion of 2 liters of saline solution at 0.9% in 4 hours. The presence of the autonomous aldosterone secretion was considered when serum aldosterone was > 5 ng/dL after the administration of the saline solution0, a value adopted by other studies published in the literature[5,23].

Only one patient, (0.96% of the total sample and 14.3% of the refractory hypertensive individuals) had a confirmed autonomous aldosterone secretion and, consequently, the diagnosis of PHA (13.1 ng/dL x 6.6 ng/dL, pre-infusion and post-infusion aldosterone, respectively).

For the etiologic differentiation of the PHA, an adrenal CT was performed with 3-mm thick slices. The CT results were considered normal. This outcome is in concordance with the study carried out by the Mayo Clinic, in which none of the hypertensive and normokalemic patients with a positive triage test for PHA presented adrenal tumors at the CT[21].

This can be explained by the high incidence of adrenal hyperplasia detectable only at the histological analysis of the gland. Thus, the absence of a radiologic substrate does not invalidate the diagnosis of PHA, if the biochemical evidence is conclusive[8].

The gold-standard assessment to differentiate adrenal tumors from adrenal hyperplasia is the selective adrenal vein catheterism, with blood collection for the measurement of aldosterone and cortisol. It is an expensive, invasive diagnostic method, which is not available in many Centers and that is technically difficult to be performed. Therefore, it was not performed in the present study.

Among the study limitations, one can cite the fact that the sample was selected by convenience and in a university hospital. Despite the consecutive inclusion, patient selection in institutions such as hospitals does not involve individuals from other Centers and the results reflect the experience of the Service itself, which cannot be generalized for the community and for the clinical practice in medical offices. Additionally, one must not forget that the triage was carried out while patients were undergoing treatment with anti-hypertensive drugs, with all the possible drug effects on the PRA, especially the ACEI in association with the thiazide diuretics. This association might have been responsible for the increase in the PRA, generating false-negative results.

As for the clinical relevance of the study, the fact that it is an original study is noteworthy, as there are neither local nor regional publications on the subject.

## Conclusion

The prevalence of PHA in the SAH League of the University Hospital of the study, when considering the entire sample, was 0.96%. However, when evaluating only the patients with refractory arterial hypertension, this prevalence reached 14.3%. Finally, when evaluating the advantages and disadvantages of using the aldosterone/PRA ratio as a triage method for the diagnosis of PHA, especially the lack of standardization of the triage test, the lack of an established cutoff, the influence of PRA (and of all the variables that affect it: sex, age, SAH, medications), in addition to its insufficiency as a diagnostic method, leading to the need of performing other, more expensive and invasive tests, one concludes that it must not be used routinely for the unsystematic evaluation of all hypertensive individuals. The PHA investigation must be carried out in hypertensive patients with hypokalemia, refractory to the usual treatment of arterial hypertension and the ones who present incidentalomas.

### Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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### Study Association

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## References

1. Kater CE. Hiperaldosteronismo primário: novas tendências. Rev Bras Hipertens., 2002; 9: 165-73.
2. Young WF Jr. Primary aldosteronism: management issues. Ann N Y Acad Sci. 2002; 970: 61-76.
3. Mulatero P, Stowasser M, Loh KC, Fardella CE, Gordon RD, Mosso L, et al. Increased diagnosis of primary aldosteronism, including surgically correctable forms, in centers from five continents. J Clin Endocrinol Metab. 2004; 89: 1045-50.
4. Francishetti EA, Abreu VG. Investigações diagnósticas em hipertensão arterial – hiperaldosteronismo. In: Sociedade Brasileira de Cardiologia. I.II Hipertensão arterial: programa de educação continuada. Rio de Janeiro:

Diagraphic; 2002. p. 6-7.

5. Gomez-Hernández K, Chen-Ku CH. Hiperaldosteronismo primario, una nueva perspectiva. Acta Méd Costarric. 2007; 49: 12-20.
6. Kaplan NM. Is there an unrecognized epidemic of primary aldosteronism? (Con). Hypertension. 2007; 50: 454-8.
7. Giacchetti G, Ronconi V, Lucarelli G, Boscaro M, Mantero F. Analysis of screening and confirmatory tests in the diagnosis of primary aldosteronism: need for a standardized protocol. J Hypertens. 2006; 24: 737-45.
8. Mosso LG, Fardella C, Montero J, Rojas P, Sánchez O, Rojas V, et al. Alta prevalência de hiperaldosteronismo primario no diagnosticado en hipertensos catalogados como esenciales. Rev Méd Chil. 1999; 127: 800-6.
9. Loh KC, Koay ES, Khaw MC, Emmanuel SC, Young WF Jr. Prevalence of primary aldosteronism among asian hypertensive patients in Singapore. J Clin Endocrinol Metab. 2000; 85: 2854-9.
10. Nishizaka MK, Ubunama MP, Zaman MA, Cofield S, Calhoun DA. Validity of plasma aldosterone-to-renin activity ratio in african american and white subjects with resistant hypertension. Am J Hypertens. 2005; 18: 805-12.
11. Umpierrez GE, Cantey P, Smiley D, Palacio A, Temponi D, Luster K, et al. Primary aldosteronism in diabetic subjects with resistant hypertension. Diabetes Care. 2007; 30: 1699-703.
12. Calhoun DA. Is there an unrecognized epidemic of primary aldosteronism? (Pro). Hypertension. 2007; 50: 447-53.
13. Mulatero, P.; Rabbia, F.; Milan, A.; Paglieri, C.; Morello, F.; Chiandussi, L. et al. Drug effects on aldosterone / plasma renin activity ratio in primary aldosteronism. Hypertension. 2002; 40: 897-908.
14. Passos VQ, Martins LAL, Pereira MAA, Kater CE. Hiperaldosteronismo primário revisitado. Arq Bras Endocrinol Metab. 2001; 45: 285-301.
15. Kater CE. Hiperaldosteronismo primário. Arq Bras Endocrinol Metab. 2002; 46: 106-15.
16. Rossi GP, Bernini G, Caliumi C, Desideri G, Fabris B, Ferri C, et al. A prospective study of the prevalence of primary aldosteronism in 1125 hypertensive patients. J Am Coll Cardiol. 2006; 48: 2293-300.
17. Fogari R, Preti P, Zoppi A, Rinaldi A, Fogari E, Mugellini A. Prevalence of primary aldosteronism among unselected hypertensive patients: a prospective study base don the use of an aldosterone / renin ratio above 25 as a screening test. Hypertens Rev. 2007; 30: 111-7.
18. Williams JS, Williams GH, Raji A, Jeunemaitre X, Brown NJ, Hopkins PN, et al. Prevalence of primary hyperaldosteronism in mild to moderate hypertension without hypokalemia. J Hum Hypertens. 2006; 20: 129-36.
19. Mulatero P, Dluhy RG, Giacchetti G, Boscaro M, Veglio F, Stewart PM. Diagnosis of primary aldosteronism: from screening to subtype differentiation. Trends Endocrinol Metab. 2005; 16: 114-9.
20. Stowasser M, Gordon RD. Primary aldosteronism – careful investigation is essential and rewarding. Mol Cell Endocrinol. 2004; 217: 33-9.
21. Krakoff LR. Screening for primary aldosteronism: progress and frustration. J Hypertens. 2006; 24: 635-7.
22. Kaplan NM. The current epidemic of primary aldosteronism: causes and consequences. J Hypertens. 2004; 22: 863-9.
23. Tiu SC, Choi CH, Shek CC, Ng YW, Chan FKW, Ng CM, et al. The use of aldosterone – renin ratio as a diagnostic test for primary hyperaldosteronism and its test characteristics under different conditions of blood sampling. J Clin Endocrinol Metab. 2005; 90: 72-8.