

# Type 2 diabetic patients with resistant hypertension should be screened for primary aldosteronism

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## Abstract

BP control in diabetic patients is often poor. The contribution of secondary hypertension due to undiagnosed PA in hypertensive type 2 diabetic patients is not well studied. We prospectively screened 100 consecutive Asian type 2 diabetic patients with difficult-to-control or resistant hypertension for PA. PAC (pmol/L) to PRA (ng/mL/h) ratio was measured; those with PAC-to-PRA ratio >550 (corresponding PAC >415) underwent intravenous 0.9% SLT. Patients with PAC  $\geq$  140 following SLT had CT adrenals and bilateral AVS. Thirteen patients (13%) were confirmed to have PA, and all had resistant hypertension. Eight had a surgically correctable form of PA. Patients with PA had higher mean (SD) systolic [159.0 (10.6) vs. 146.0 (10.7) mmHg,  $p=0.001$ ] and diastolic BP [94.6 (6.0) vs. 87.6 (5.9) mmHg,  $p=0.001$ ], lower serum potassium [3.5 (0.6) vs. 4.3 (0.5) mmol/L,  $p=0.001$ ], and higher PAC [679.3 (291.0) vs. 239.5 (169.4) pmol/L,  $p=0.001$ ]. Identification and institution of definitive treatment for PA resulted in better BP control and in a reduction in the use of antihypertensive medications. Our findings demonstrate a high prevalence of PA in type 2 diabetic patients with resistant hypertension. Systematic screening for PA in this select group is recommended, as targeted treatment improves BP control.

## Keywords

diabetes mellitus, difficult-to-control hypertension, primary aldosteronism, resistant hypertension

## Introduction

CVD is the leading cause of morbidity and mortality in patients with type 2 diabetes mellitus.<sup>1</sup> Hypertension, one of the major independent risk factors for CVD, is more prevalent amongst diabetics.<sup>2,3</sup> Tight BP control in type 2 diabetic patients not only significantly reduces the incidence of microvascular complications, but also reduces the incidence of cardiovascular complications such as heart failure and stroke.<sup>4</sup> However, despite this compelling evidence, the number of diabetics who achieve target BP is dismal, with approximately 50–75% failing to achieve good BP control.<sup>5,6</sup>

Diabetic nephropathy, hyperinsulinaemia<sup>7</sup> and extracellular volume expansion<sup>8</sup> have been proposed to contribute to hypertension in diabetic patients. However, the contribution of excess aldosterone in the pathogenesis of hypertension in patients with type 2 diabetes mellitus remains unknown. Aldosterone is principally involved in the maintenance of sodium and water homeostasis. Excess aldosterone, as seen in patients with PA, leads to excess sodium and water retention, and eventual hypertension. PA is now recognised as the commonest cause of secondary hypertension.<sup>9</sup> Importantly, early diagnosis and treatment of PA offers a potential cure for hypertension.

Recent evidence suggests that there are a lot of similarities between the deleterious effects of excess aldosterone and hyperglycaemia on various cardiovascular parameters, which eventually promote CVD. For example, in animal and clinical studies, both hyperglycaemia and aldosterone have been shown to induce myocardial fibrosis, and cause left ventricular hypertrophy and remodelling.<sup>10–13</sup> Aldosterone stimulates the production and expression of plasma activator inhibitor 1, promotes oxidative stress, reduces the endothelial production of nitric oxide and increases adhesion of platelets, monocytes and leukocytes, which together contribute to inflammation and vasculopathy; similar effects are seen with hyperglycaemia.<sup>2,14</sup> In addition, aldosterone

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decreases baroreflex sensitivity and enhances sympathetic activity,<sup>15</sup> abnormalities that might contribute to hypertension in diabetes mellitus. Indeed, the prevalence of cardiovascular events is greater in patients with PA than in those with essential hypertension,<sup>16</sup> further suggesting a pathological role of excess aldosterone in CVD, independent of BP.

There is accumulating evidence to suggest a close relationship between aldosterone excess and insulin resistance. Aldosterone promotes insulin resistance via defects in insulin signalling and glucose uptake in the skeletal tissue.<sup>17, 18</sup> A high prevalence of glucose intolerance and/or diabetes mellitus has also been reported in patients with PA.<sup>19, 20</sup> On the other hand, hyperinsulinaemia, a feature of insulin resistance, is known to stimulate the production of aldosterone.<sup>21, 22</sup> Since patients with diabetes mellitus and hypertension are typically insulin-resistant, it has been postulated that excess aldosterone may contribute to poorly controlled hypertension in patients with diabetes mellitus.<sup>18</sup> It is thus probable that the prevalence of PA might be higher in hypertensive type 2 diabetic patients.

The primary aim of our study was to examine the prevalence of PA in diabetic patients with poorly controlled hypertension in the Asian context. To date, there is only one published study that suggests a high prevalence of PA amongst diabetic patients with resistant hypertension.<sup>23</sup> Early diagnosis and treatment of PA might reduce the burden of CVD in type 2 diabetic patients.

## Research design and methods

This study aimed to screen for PA in adult diabetic patients with poorly controlled hypertension. We enrolled 100 consecutive type 2 diabetic patients with difficult-to-control or resistant hypertension. The patients were recruited from those attending the Diabetes Centre at the National University Hospital, Singapore, over a period of one year from July 2004 to June 2005. Exclusion criteria included the presence of elevated serum creatinine value greater than 160  $\mu\text{mol/L}$ , pregnancy or breast-feeding, history of congestive cardiac failure, known pheochromocytoma or Cushing's syndrome. All patients were on stable antihypertensive medications for at least four weeks before evaluation. None of these patients were on treatment with either Spironolactone or Epleronone. The study was approved by the local ethics committee.

Following written informed consent, all patients gave a detailed history and underwent physical examination and anthropometric measurements. BP was measured using a mercury sphygmomanometer with the patient sitting, after 15 min of rest. In the event that BP was  $>140/90$  mmHg, repeat measurements were taken using a sphygmomanometer with the patient sitting on two further occasions, 5 min apart, and the average of the last two readings was used for data analysis.

As described by Moser and Setaro,<sup>24</sup> difficult-to-control hypertension was defined as BP  $>140/90$  mmHg despite taking two different classes of antihypertensive medications for at least three months or requiring three or more different classes of antihypertensive medications for BP control. Resistant hypertension was defined as BP  $>140/90$  mmHg despite adherence to optimum treatment with three or more different classes of antihypertensive medications.

## Screening and diagnosis of PA

Fasting blood samples were drawn in the morning, with the patient in a sitting position, after having rested for 30 min. Blood was collected for measurement of serum potassium, serum creatinine, HbA<sub>1c</sub>, PAC (pmol/L) and PRA (ng/mL/h).

PAC-to-PRA ratio was calculated in all patients. Patients with a positive screening test, defined as PAC-to-PRA ratio  $>550$  (with a corresponding PAC value  $>415$  pmol/L), underwent a confirmatory 4-h intravenous 0.9% SLT. During this test, PAC was measured 4 h after the intravenous administration of 2 litres of 0.9% saline at the rate of 500 mL/h. Patients with a PAC value  $\geq 140$  pmol/L following SLT (post-PAC) underwent further investigations, including CT with fine cuts (3 mm) of the adrenals, and bilateral AVS for PAC, to determine the aetiology of PA. Adrenal vein cannulation was considered successful if the adrenal vein/inferior vena cava cortisol gradient was at least two, and was considered to show lateralisation when the aldosterone/cortisol ratio in one adrenal vein was at least four times the ratio in the other adrenal vein.<sup>25</sup>

## Laboratory measurements

All hormonal assays were performed in the biochemistry laboratory at the National University Hospital, Singapore, which is accredited by the College of American Pathologists. PAC was measured using a solid-phase 125-I RIA (Siemens Medical Solutions Diagnostics, LA, USA); the intra-assay and inter-assay CV for PAC were 3.4% and 6.5%, respectively. PRA was measured by quantifying angiotensin I, generated after incubation of plasma, by standard RIA (DiaSorin, Stillater, MN, USA); the intra-assay and inter-assay CV for PRA were 4.6% and 7.6%, respectively. The reference ranges for upright PAC and PRA were 110–860 pmol/L and 1.31–3.95 ng/mL/h respectively. HbA<sub>1c</sub> was measured using an ion exchange chromatography method (Variant II, Bio-Rad Laboratories).

## Statistical analysis

All values are expressed as means  $\pm$  SD unless otherwise noted. Comparisons of continuous variables between patients with and without PA were carried out using Student t test. A two-tailed  $p < 0.05$  was considered significant.

**Table 1.** Clinical characteristics of 100 type 2 diabetic patients with poorly controlled hypertension

	All patients	Patients without PA	Patients with PA	p-value
N	100	87	13	
Age (years)	57.4 ± 9.7	57.0 ± 9.9	60.2 ± 7.9	NS
BMI (kg/m <sup>2</sup> )	28.0 ± 4.4	28.2 ± 4.6	26.2 ± 2.6	NS
Duration of DM (years)	11.4 ± 7.8	11.9 ± 8.0	8.6 ± 5.9	NS
Duration of HTN (years)	12.8 ± 8.6	12.2 ± 8.2	16.2 ± 10.8	NS
Systolic BP (mmHg)	147.8 ± 11.6	146.0 ± 10.7	159.0 ± 10.6	0.001
Diastolic BP (mmHg)	88.5 ± 6.4	87.6 ± 5.9	94.6 ± 6.0	0.001
Number of BP medications	3.0 ± 0.8	2.9 ± 0.8	3.4 ± 0.7	NS
Number of patients on two AHTs	28	28	0	
Number of patients on three AHTs	49	40	9	
Number of patients on four AHTs	18	15	3	
Number of patients on five AHTs	5	4	1	
Number of patients taking a particular BP medication				
ACE inhibitor and/or ARB	96	83	13	
Diuretic	52	47	5	
Beta blocker	81	68	13	
Calcium channel blocker	53	45	8	
Alpha blocker	2	1	1	
Others	1	0	1	
Potassium (mmol/L)	4.2 ± 0.6	4.3 ± 0.5	3.5 ± 0.6	0.001
HbA <sub>1c</sub> (%)	7.8 ± 1.3	7.8 ± 1.3	7.7 ± 1.7	NS
PAC (pmol/L)	296.7 ± 239.3	239.5 ± 169.4	679.3 ± 291.0	<0.001
PRA (ng/mL/h)	4.32 ± 6.00	4.91 ± 6.22	0.34 ± 0.24	<0.001
PAC-to-PRA ratio	601.2 ± 864.4	345.0 ± 539.6	2,315.8 ± 645.8	<0.001

Key: Data are expressed as mean ± SD unless stated otherwise. ACE = angiotensin converting enzyme; AHT = antihypertensive medication; ARB = angiotensin receptor blocker; BMI = body mass index; BP = blood pressure; DM = diabetes mellitus; HbA<sub>1c</sub> = glycosylated haemoglobin; HTN = hypertension; NS = non-significant; PA = primary aldosteronism; PAC = plasma aldosterone concentration; PRA = plasma renin activity; SD = standard deviation

Statistical analysis was performed with SPSS (version 13.0 for Windows; SPSS Inc., Chicago, IL).

## Results

### Clinical characteristics of 100 hypertensive type 2 diabetic patients (tables 1 and 2)

The baseline clinical characteristics of all 100 type 2 diabetic patients are shown in tables 1 and 2. The study patients had a mean (SD) age of 57.4 (9.7) years, and 46% were male. The mean (SD) duration of diabetes and hypertension were 11.4 (7.8) and 12.8 (8.6) years respectively. Fifty-two patients had difficult-to-control hypertension and 48 had resistant hypertension. The mean (SD) systolic and diastolic BP were 147.8 (11.6) and 88.5 (6.4) mmHg respectively. Thirteen patients (13%) were confirmed to have PA, and all of them had resistant hypertension.

### Clinical characteristics of the 13 patients with confirmed PA (table 1)

There was no difference in age, BMI, duration of diabetes or hypertension, HbA<sub>1c</sub>, and number of antihypertensive

medications used between the patients with and without PA. Patients with PA had higher mean systolic and diastolic BP but lower mean serum potassium than patients without PA. Serum potassium was measured in all patients during the initial screening visit when none were on potassium supplements. Six (46%) patients had a screening serum potassium value lower than 3.5 mmol/L.

The patients with PA had higher mean PAC (679.3 vs. 239.5 pmol/L,  $p < 0.001$ ), lower PRA (0.34 vs. 4.91 ng/mL/h,  $p < 0.001$ ), and higher PAC-to-PRA ratio (2,315.8 vs. 345.0,  $p < 0.001$ ) when compared with those without PA.

### Subtype differentiation amongst 13 patients with PA (table 2)

Of the 13 patients with confirmed PA, eight had a surgically correctable form of PA: seven had a unilateral APA and one had primary adrenal hyperplasia. Of the remaining five patients, four had BAH, and in one the aetiology remained indeterminate.

Of the seven patients with confirmed APA, six had a unilateral adrenal adenoma visible on CT scan (size ranging from 1.0 cm to 2.6 cm), and one had bilateral adrenal nodules (2.6 cm in the left, and 0.6 cm in the

**Table 2.** Clinical characteristics and subtype differentiation of 13 patients with primary aldosteronism

	APA	BAH	PAH	Undetermined
N	7	4	1	1
Age (years)	59.0 ± 3.0	62.0 ± 4.2	69.0	52.0
BMI (kg/m <sup>2</sup> )	27.1 ± 1.3	25.3 ± 0.6	24.4	25.3
Duration of DM (years)	8.7 ± 1.9	10.5 ± 3.9	8.0	0.5
Duration of HTN (years)	14.4 ± 3.0	15.0 ± 5.6	40.0	10.0
Number of antihypertensive medications	3.4 ± 0.3	3.2 ± 0.2	4.0	3.0
Potassium (mmol/L)	3.5 ± 0.3	3.7 ± 0.2	3.4	2.8
HbA <sub>1c</sub> (%)	7.9 ± 0.7	7.8 ± 1.0	6.9	6.5
PAC (pmol/L)	739.0 ± 375.2	569.5 ± 86.9	884.0	496.0
PRA (ng/mL/h)	0.38 ± 0.31	0.28 ± 0.16	0.4	0.2
PAC-to-PRA ratio	2,276.1 ± 752.1	2,325.0 ± 722.7	2,389	3,307
PAC post-SLT (pmol/L)	358.0 ± 76.3	379.0 ± 83.2	230.0	639.0
Number who underwent AVS	6	4	1	1
Number with unequivocal lateralisation on AVS	6	0	1	1
Number who underwent unilateral adrenalectomy	5	0	1	0

Key: Data are expressed as mean ± SD unless stated otherwise. APA = aldosterone-producing adenoma; AVS = adrenal venous sampling; BAH = bilateral adrenal hyperplasia; BMI = body mass index; DM = diabetes mellitus; HbA<sub>1c</sub> = glycosylated haemoglobin; HTN = hypertension; PAC = plasma aldosterone concentration; PAH = primary adrenal hyperplasia; PRA = plasma renin activity; SD = standard deviation; SLT = saline loading test

right adrenal gland). Six of the seven patients with APA underwent AVS, which lateralised the source of aldosterone secretion to the side of the visible adenoma in the five with unilateral adenoma, and to the left side in the patient with bilateral adrenal nodules. Five patients have undergone unilateral adrenalectomy; histology confirmed an adrenal adenoma. Post-adrenalectomy, all five had normalisation of previously noted low serum potassium values that had earlier necessitated potassium replacement, together with improvement in hypertension control, with not only fewer, but also reduced dosages of, antihypertensive medications. The other two patients with APA (one with poor cardiac function, and another, a 65-year-old woman, with a visible 1.3 cm adenoma on the left adrenal gland, who refused surgery) are on spironolactone with good BP control.

One patient with PA, a 69-year-old man, had a hyperplastic right adrenal gland with a 0.8 cm nodule visible within this gland on CT scan. The left adrenal gland was normal. AVS lateralised the source of excess aldosterone secretion to the right side. He underwent right adrenalectomy. Histology revealed an adrenal gland with small focal areas of cortical hyperplasia with a few small cortical nodules, the largest measuring 2 mm in diameter. No definite adenoma was identified, a finding consistent with primary adrenal hyperplasia. Similar to the response seen in the five patients with APA treated surgically, following unilateral laparoscopic adrenalectomy, there was normalisation of previously noted low serum potassium values in this patient, together with improvement in his BP control.

All four patients with BAH had hyperplastic adrenal glands on CT scan. AVS failed to lateralise the source of

aldosterone secretion in all four patients. They were treated with spironolactone, with good BP control.

The subtype of the last patient with confirmed PA remained indeterminate. Although both adrenal glands appeared hyperplastic on CT scan, AVS lateralised the source of aldosterone secretion to the right side. However, in the absence of a visible nodule on imaging, the patient refused adrenalectomy, and preferred follow-up whilst on spironolactone for BP control.

## Discussion

Diabetes mellitus and hypertension constitute two powerful independent risk factors for cardiovascular, renal and atherosclerotic disease.<sup>26, 27</sup> Better control of hypertension in diabetic patients is crucial in order to reduce the risk of cardiovascular morbidity and mortality.<sup>4</sup> The benefits of tight BP control in diabetic patients were conclusively demonstrated by the UKPDS,<sup>28</sup> and further reinforced by the findings in the HOT trial, which revealed that a 4 mmHg reduction in diastolic BP led to an impressive 51% risk reduction in CVD.<sup>29</sup> Despite this compelling evidence, only a minority of diabetic patients achieve target BP of 130/80 mmHg.<sup>5</sup> Poor patient compliance, cost and side effects of antihypertensive medications, presence of co-morbidities, and physicians' lack of adherence to practice guidelines for managing hypertension are often cited as the principal reasons for poorly controlled hypertension in diabetic patients.<sup>30</sup> The contribution of undiagnosed PA to the failure to achieve good BP control in type 2 diabetic patients is relatively unknown.

**Table 3.** Prevalence of primary aldosteronism in unselected hypertensive adults and in hypertensive type 2 diabetic patients

Author	Year	Number screened	Type of patients	Prevalence	
				N	%
Hiramatsu <i>et al.</i> <sup>35</sup>	1981	348	Unselected hypertensives	9	2.6
Gordon <i>et al.</i> <sup>34</sup>	1994	199	Unselected hypertensives	17	8.5
Lim <i>et al.</i> <sup>36</sup>	1999	465	Unselected hypertensives	43	9.2
Loh <i>et al.</i> <sup>37</sup>	2000	350	Unselected hypertensives	16	4.6
Fardella <i>et al.</i> <sup>33</sup>	2000	305	Unselected hypertensives	29	9.5
Calhoun <i>et al.</i> <sup>42</sup>	2002	88	Resistant hypertensives	18	20
Mosso <i>et al.</i> <sup>32</sup>	2003	301	Mild hypertension	6	2.0
		187	Moderate hypertension	15	8.0
		121	Severe hypertension	16	13.2
Total		609	Unselected hypertensives	37	6.1
Schwartz and Turner <sup>43</sup>	2005	118	Unselected hypertensives	15	13
Williams <i>et al.</i> <sup>39</sup>	2006	347	Unselected hypertensives	11	3.2
Westerdahl <i>et al.</i> <sup>38</sup>	2006	200	Unselected hypertensives	17	8.5
Rossi <i>et al.</i> <sup>44</sup>	2006	1125	Unselected hypertensives	126	11.2
Umpierrez <i>et al.</i> <sup>23</sup>	2007	100	Diabetics with resistant hypertension	14	14.0
Douma <i>et al.</i> <sup>45</sup>	2008	1616	Resistant hypertensives	182	11.3
Our study	2009	100	Hypertensive diabetics	13	13.0

In this study, we found a 13% prevalence of PA in 100 consecutive type 2 diabetic patients with poorly controlled hypertension. All 13 patients with PA had resistant hypertension. Our findings are in keeping with the only other published study that looked at the prevalence of PA in type 2 diabetic patients with resistant hypertension; they found a similar prevalence at 14%.<sup>23</sup> Importantly, definitive treatment of PA in our study, with either surgical removal of the adrenal APA or blockade with an aldosterone antagonist, resulted in better BP control and a reduction in the use of antihypertensive medications.

Studies over the past decade have demonstrated a 3%–13% prevalence of PA in unselected adult hypertensive patients, with a higher prevalence in patients with more severe hypertension (table 3).<sup>31</sup> In a study by Mosso *et al.*,<sup>32</sup> the prevalence of PA increased with the severity of hypertension, being 2% in patients with mild hypertension, 8% in patients with moderate hypertension, and 13.2% in patients with severe hypertension. As discussed earlier, it is probable that the prevalence of PA might be higher in hypertensive type 2 diabetic patients. Indeed, the prevalence of 13% seen in our study is higher than that reported in most studies evaluating the prevalence of PA in unselected adult hypertensive patients (table 3),<sup>33–39</sup> though it seems comparable to 13.2%, reported by Mosso *et al.*<sup>32</sup> amongst patients with severe hypertension. In the absence of a control group of non-diabetic hypertensive subjects, it is difficult to comment on whether the observed prevalence in our study is indeed higher than that seen in the non-diabetic hypertensive population. A previous study from Singapore, conducted

in an unselected adult hypertensive population, had reported a 5% prevalence of PA.<sup>37</sup> In contrast, in our study, the prevalence rate was higher, at 13%. However, the higher prevalence seen in our cohort could also be explained by the fact that the patients in our cohort had more severe hypertension than in this earlier study from Singapore; three-quarters of the patients in this earlier study were taking a single antihypertensive medication, with the majority of the remaining patients taking two drugs, as opposed to all patients in our cohort having either difficult-to-control or resistant hypertension. Further studies that directly compare the prevalence of PA in diabetic vs. non-diabetic hypertensive patients are needed to confirm whether the prevalence is indeed higher amongst hypertensive type 2 diabetic patients.

In recent years, we have gathered more insights into the role of aldosterone and its potential adverse effects on the cardiovascular system, independent of its effect on BP. Patients with PA are at higher risk of stroke, myocardial infarction, atrial fibrillation and left ventricular hypertrophy than matched individuals with essential hypertension.<sup>16</sup> Additionally, a higher prevalence of metabolic syndrome and greater insulin resistance have been demonstrated in patients with PA.<sup>40,41</sup> These metabolic abnormalities were corrected following the removal of the APA.<sup>19, 20</sup> Taken together with the findings of the study by Umpierrez *et al.*,<sup>23</sup> our study reinforces the need to screen for PA in type 2 diabetic patients with resistant hypertension.

The major strength of our study was the systematic approach employed to follow up on positive screening PAC-to-PRA ratios. We performed a confirmatory 4-h

0.9% SLT and CT imaging of the adrenals in all, and bilateral AVS in 12, of the 13 patients with confirmed PA. Of the 13 patients with PA in our study, eight had a surgically correctable form of PA, and six of these have undergone adrenalectomy. The remaining seven patients, including two with APA, four with BAH, and one who remained indeterminate, were on spironolactone with good BP control.

We acknowledge several limitations of our study. The first limitation concerns the difficulty in interpreting the PAC-to-PRA ratio in patients receiving medications that interfere with the renin–angiotensin–aldosterone system. It is often not possible to safely withdraw antihypertensive medications for 2–4 weeks in patients with difficult-to-control or resistant hypertension. The false positive screening tests due to the use of beta blockers would have been weeded out by the use of the confirmatory 4-h intravenous 0.9% SLT. Diuretics, ACE inhibitors, and angiotensin 2 receptor blockers might have resulted in false negative PAC-to-PRA ratios; we did not perform a confirmatory 4-h intravenous 0.9% SLT in all 100 patients, and this might have led to our inability to identify these patients with a false negative PAC-to-PRA ratio, potentially leading to an underestimation of the prevalence of PA in our cohort. Also, we chose a PAC-to-PRA ratio greater than 550 pmol/L per ng/mL per h, together with a corresponding PAC greater than 415 pmol/L, to constitute a positive screening test. This might have excluded a few patients with PA who had an elevated PAC-to-PRA ratio but a corresponding PAC of less than 415 pmol/L. The other limitation, as discussed earlier, was the lack of a control group of non-diabetic hypertensive subjects. Although this does not affect the prevalence of PA noted in our study, it does not allow us to comment on whether the observed prevalence in our study is indeed higher than that seen in the non-diabetic hypertensive population.<sup>23,32,42</sup>

In summary, undiagnosed PA might account for 13% of type 2 diabetic patients with resistant hypertension. Identification and treatment of this reversible cause of hypertension in type 2 diabetic patients would have a tremendous impact on achieving BP control, allowing significant reduction in long-term cardiovascular morbidity and mortality. We therefore recommend that all type 2 diabetic patients with resistant hypertension be screened for the presence of PA.

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### Abbreviations

adrenal venous sampling	AVS
aldosterone-producing adenoma	APA
angiotensin converting enzyme	ACE
bilateral adrenal hyperplasia	BAH
blood pressure	BP
body mass index	BMI
cardiovascular disease	CVD
coefficient of variation	CV
computed tomography	CT
glycosylated haemoglobin	HbA <sub>1c</sub>
Hypertension Optimal Treatment	HOT
plasma aldosterone concentration	PAC
plasma renin activity	PRA
primary aldosteronism	PA
radioimmunoassay	RIA
saline loading test	SLT
standard deviation	SD
United Kingdom Prospective Diabetes Study	UKPDS

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