# Computed tomography and adrenal venous sampling in the diagnosis of unilateral primary aldosteronism

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**Abstract**

Unilateral primary aldosteronism is the most common surgically correctable form of endocrine hypertension and is usually differentiated from bilateral forms by adrenal venous sampling or computed tomography. Our objective was to compare clinical and biochemical post-surgical outcomes of patients with unilateral primary aldosteronism diagnosed by computed tomography or adrenal venous sampling and identify predictors of surgical outcomes. Patient data were obtained from 18 internationally distributed centres and retrospectively analysed for clinical and biochemical outcomes of adrenalectomy of patients with surgical management based on computed tomography (n=235 patients, diagnosed from 1994 to 2016) or adrenal venous sampling (526 patients, diagnosed from 1994 to 2015) using the standardised Primary Aldosteronism Surgical Outcome criteria. Biochemical outcomes were highly different according to surgical management approach with a smaller proportion in the computed tomography group achieving complete biochemical success (188 of 235 [80%] patients *versus* 491 of 526 [93%], p<0.001) and a greater proportion with absent biochemical success (29 of 235 [12%] *versus* 10 of 526 [2%], p<0.001). A diagnosis by computed tomography was associated with a decreased likelihood of complete biochemical success compared with adrenal venous sampling (OR 0.28, 0.16-0.50; p<0.001). Clinical outcomes were not significantly different but the absence of a post-surgical elevated aldosterone-to-renin ratio was a strong marker of complete clinical success (OR 14.81, 1.76-124.53; p=0.013) in the computed tomography but not in the adrenal venous sampling group. In conclusion, patients diagnosed by computed tomography

have a decreased likelihood of achieving complete biochemical success compared with a diagnosis by adrenal venous sampling.

**Key words**

Primary aldosteronism, adrenal venous sampling, aldosterone producing adenoma, bilateral adrenal hyperplasia, adrenalectomy, endocrine hypertension

## Introduction

Primary aldosteronism (PA) is a frequent cause of secondary hypertension with a reported prevalence of 5-10% in unselected populations and up to 20% in patients with resistant hypertension.[1-5] The excess aldosterone production that causes the disorder may be unilateral (confined to one adrenal) or bilateral and the two forms are preferentially treated by unilateral adrenalectomy or a mineralocorticoid receptor antagonist, respectively.[6, 7] Unilateral PA is the most common surgically correctable cause of hypertension with a highly variable proportion of patients achieving clinical remission after surgery between centres.[8-10]

Patients with PA have a widely reported increased risk of prevalent cardiovascular and cerebrovascular complications and target organ damage relative to matched patients with primary hypertension who have otherwise similar cardiovascular risk profiles or compared with the general population with hypertension.[11-17] An increasing body of evidence implies that an early diagnosis and targeted treatment can minimise or reverse the increased risks associated with this condition. Failure to identify those with unilateral forms constrains patients with unilateral disease to a lifetime of medical treatment instead of offering a potential surgical cure and has an impact on quality of life.[18-21]

The accurate differention of unilateral from bilateral PA is therefore mandatory for optimal clinical management and is widely undertaken by adrenal venous sampling (AVS) and/or an imaging technique, usually adrenal computed tomography (CT) or magnetic resonance. AVS determines whether one or both

adrenals are responsible for aldosterone excess. The ability of AVS to provide functional information regarding the source of aldosterone overproduction in PA might be expected to render it superior in terms of diagnostic accuracy than imaging techniques such as CT which provide only structural information. Indeed, CT has been widely reported to be unreliable for differentiation of unilateral from bilateral PA, lacks sensitivity for the detection of microadenomas (<10 mm diameter) and specificity in patients with non-functional adrenal incidentalomas.[6, 22-27] For these reasons AVS is recommended for the diagnostic work up of PA by the clinical practice guideline of the Endocrine Society.[6] The only randomised prospective clinical trial that compared AVS and CT in the differentiation of unilateral from bilateral PA found no significant differences in clinical outcomes between the two approaches. A non-significant difference in biochemical outcomes (80% biochemical remission in the CT *versus* 89% in the AVS group) and health-related quality of life was also reported and the study concluded that the reference standard status of AVS in the diagnostic work up of PA was unjustified.[28]

Our objective was to evaluate the diagnostic value of CT compared with AVS for unilateral PA in a large international cohort of patients retrospectively assessed for clinical and biochemical outcomes by the international primary aldosteronism surgical outcome (PASO) consensus[10] and to identify predictors of outcomes.

## Methods

The authors declare that all supporting data are available within the article and its online supplementary files.

*An expanded Methods section is available in the online-only data supplement*

### Patient cohorts and outcome assessment

All 12 centres from the PASO study were invited to contribute patient data based on AVS surgical management, of which 9 accepted (Berlin, Brisbane, Kyoto, Ljubljana, Munich, Sendai, Torino, Warsaw, Yokohama). Data from 761 patients with unilateral PA were obtained (235 with CT management diagnosed from 1994 to 2016, and 526 with AVS management diagnosed from 1994 to 2015) (Table S1, Figure S1). The patients in the AVS group are a subset of the patients from the PASO study with the addition of CT data and 4 extra patients (2 in Munich and 2 in Berlin) due to newly available outcome data. The CT group included all patients in each centre with a diagnosis of unilateral PA by CT in the study period (Figure S1). In this group, unilateral PA was diagnosed if a unilateral nodule of at least 8 mm in diameter was detected. Clinical and biochemical outcomes were assessed retrospectively in accordance with the standardised criteria of the PASO consensus with follow-up at 6-12 months which are based on blood pressure measurements and antihypertensive drug dosage (clinical outcomes) and assessment of the aldosterone-to-renin ratio and normalisation of hypokalemia (if present pre-surgically) (biochemical outcomes).[10] PA was diagnosed by the US Endocrine Society guideline or the Japan Endocrine Society guideline.[6, 29] All details on patient inclusion and assessment are provided in the online-only data supplement. The study was

approved by an institutional review board with patient data and written informed patient consent obtained in accordance with local ethical guidelines.

### Statistical analyses

Data are expressed as absolute numbers and percentages, means with standard deviations (SD) or as medians with interquartile ranges (IQR) as appropriate. IBM SPSS statistics version 22.0 was used for all analyses. P values <0.05 were considered significant. Details of all statistics are given in the online-only data supplement.

## Results

*An expanded Results section is available in the online-only data supplement*

### Biochemical outcomes stratified by CT and AVS based surgical decision

The CT group comprised a smaller proportion of patients achieving complete biochemical success after surgery (cure of PA) (188 of 235 patients, 80.0%) compared with AVS (491 of 526, 93.3%) (p<0.001) and a higher proportion with absent biochemical success (12.3% *versus* 1.9%, p<0.001) and persisting PA (partial and absent biochemical success combined) (20.0% *versus* 6.7%, p<0.001) (Figure 1 and Table 1). Similar clinical and biochemical outcomes were observed when the analysis was restricted to centres using either an AVS or CT scan approach (Figure S2).

### Clinical outcomes stratified by CT and AVS based surgical decision

The proportion of patients achieving complete clinical success was similar (38.6% *versus* 37.3% in the CT and AVS groups, respectively, p=0.718) (Figure 1,

Table 1). Despite this, in the CT group, the median post-surgical aldosterone-to-renin ratio (measured with plasma renin activity [PRA] because direct renin concentration measurements may perform less well compared with PRA for low renin values)[30, 31] was highly elevated in patients with an absent clinical outcome [107.1, IQR 64.5-213.5] (Table S2) and significantly greater than in patients with either partial ($p<0.001$) or complete clinical success ($p<0.001$) (Figure 2, Table S2). Patients with AVS management displayed no significant differences in the aldosterone-to-renin ratio stratified for clinical outcomes (Figure 2, Table S4).

Assessment of post-surgical outcomes across centres indicated less variance in clinical remission (22-48%) and a wider variance in biochemical remission (67-92%) with CT managment relative to that noted previously with AVS (Figure S2).[10] There was no discernable timeline bias for the diagnosis of the patients with absent or partial biochemical success with CT surgical management (Figure S1) and these patients were not concentrated in any particular centre (Figure S3).

**Identification of factors associated with CT and AVS based surgical outcomes**

Patient characteristics were stratified for clinical and biochemical outcomes based on CT- (Tables S2 and S3) or AVS-based management (Tables S4 and S5). In agreement with the PASO study, the unadjusted analysis showed that younger age, female sex, lower body mass index (BMI) and an absence of target organ damage to kidneys and heart were factors associated with complete clinical success in the AVS group (Table S4). Three of these (younger age, female sex and

lower BMI) were also associated with complete clinical success in the CT group (Table S2).

A CT-based surgical decision was a factor associated with a lower likelihood of complete biochemical success compared with an AVS-based surgical decision (complete *versus* partial + absent: adjusted OR 0.28, 0.16-0.50; p<0.001). The approach to surgical management did not influence the likelihood clinical outcomes (Table 2).

In the total cohort the absence of an elevated aldosterone-to-renin ratio at follow-up was a factor associated with both complete clinical success (adjusted OR 4.92, 1.63-14.88; p=0.005) and clinical benefit (complete + partial clinical success combined: adjusted OR 7.46, 3.35-16.63; p<0.001) (Table 2). This marker of clinical outcome was driven by patients with CT management where the absence of an elevated post-surgical aldosterone-to-renin ratio was associated with complete clinical outcome (adjusted OR 14.81, 1.76-124.53; p=0.013) and clinical benefit (adjusted OR 45.49, 11.63-177.93; p<0.001). The aldosterone-to-renin ratio at follow-up was not associated with clinical outcome in the AVS group (Table 2).

**Reliability of CT compared with AVS for the diagnosis of unilateral primary aldosteronism including young patients below 35 years of age**

In the diagnostic work up of PA, CT scanning precedes AVS to exclude the presence of an adrenocortical carcinoma. Comparison of CT with AVS results showed discordant findings in 178 (36% of 491) patients with AVS management

(who were biochemically cured after adrenalectomy). If CT data had been used for subtype differentiation, resection of the wrong adrenal would have occurred in 9 patients (2%) and 169 patients (34%) would have missed the chance of surgery because of an inappropriate diagnosis of bilateral disease (71 patients [14%] with bilateral normal and 98 patients [20%] with bilateral abnormal adrenals) (Figure 3A).

We tested the reliability of CT management in young patients (<35 years) with specific biochemical (baseline plasma aldosterone concentration >30 ng/dL and spontaneous hypokalemia) and imaging characteristics . There were 40 (7.6% of 526) and 20 (8.5% of 235) patients aged less than 35 years of age in the AVS and CT groups, respectively. The CT results indicated that 26 of the patients in the AVS group (65% of 40, all with complete biochemical success) and 11 in the CT group (55% of 20 patients, 8 complete, 1 partial and 2 absent biochemical success) had a unilateral adrenal mass (> 10 mm diameter) with a normal appearing contralateral adrenal. These imaging results combined with a marked phenotype of PA at baseline (plasma aldosterone concentration > 30 ng/dL and spontaneous hypokalemia) were observed in 17 (12 complete and 5 partial clinical success) and 5 (2 complete, 2 partial clinical success and 1 with missing clinical data) patients aged less than 35 years, all of whom were biochemically cured by adrenalectomy.

**Discussion**

The diagnosis of unilateral PA by AVS and treatment by total unilateral adrenalectomy results in biochemical remission in more than 9 out of 10

patients and clinical remission or a marked improvement in clinical parameters in just over 4 out of 5 patients.[10] An outcome of partial or absent biochemical success after surgery defines those patients with persisting hyperaldosteronism and therefore presumably bilateral PA that was misdiagnosed as unilateral pre-operatively . The accurate diagnosis of unilateral PA that determines the therapeutic strategy is thus fundamental if a patient is to be offered the possibility of biochemical cure.

Herein we show that the likelihood of cure of aldosteronism (complete biochemical success) with AVS-based surgical management is higher relative to surgery based on adrenal CT. Although this was not accompanied by a higher likelihood of clinical cure, it is noteworthy that evidence of persisting PA (indicated by an elevated aldosterone-to-renin ratio which is a criterion of absent and partial biochemical success) in patients with a CT-based diagnosis was associated with unfavourable clinical outcomes (absent in patients with AVS management). Furthermore, it is well established that long-term excessive and autonomous aldosterone production leads to severe detrimental effects independent of blood pressure control and carries an increased risk of cardiovascular and cardiometabolic events and death relative to patients with primary hypertension.[5, 11-16] Additionally, the persistence of low plasma renin activity levels in patients with PA treated with mineralocorticoid receptor antagonists (indicating persistence of inappropriate activation of the mineralocorticoid receptor by aldosterone) are associated with unfavourable cardiovascular long term outcomes.[16] These observations highlight the clinical importance of biochemical (and not just clinical) cure and support the

recommendation of long-term yearly follow-up with both clinical and biochemical assessment in adrenalectomized patients with PA .[10, 16] Herein we report that in the group with an AVS based surgical decision, the ARR was not elevated in patients with absent clinical outcomes indicating that other factors likely determined the lack of clinical remission such as pre-existing primary hypertension, long-duration of hypertension, older age and renal insufficiency. In contrast, with CT management, persistent hyperaldosteronism was a potential additional factor that contributed to absent clinical outcomes indicated by the elevated ARR.

The main differences between our study and that of Dekkers et al.,[28] other than the retrospective observational *versus* prospective randomised design, was the assessment of outcomes in accordance with a standardised set of criteria[10] and the greater number of patients with unilateral PA included in the present study (235 and 526 patients in the CT and AVS groups respectively) compared with the prospective study (46 patients in each group). Despite these differences, the proportions of patients with complete biochemical success reported in both are highly similar (80% with a diagnosis by CT in both studies and 93% *versus* 89%, in this and in Dekkers' study, diagnosed by AVS). These observations raise the possibility that with sufficient numbers the prospective SPARTACUS study would also have demonstrated significant differences in surgical outcomes between the CT- and AVS-based treatment groups, as acknowledged by Dekkers et al.[28]

The present study is the largest cohort to date that employs uniform (albeit post hoc) follow up data assessed in accordance with an international consensus.[10]

We demonstrate the lower performance of non-functional imaging compared with AVS for the diagnosis of lateralised aldosterone excess in unilateral PA. The high level of discordance between imaging and AVS results for determining lateralisation in PA has been reported previously.[25, 32] Our data also support the concept that adrenal CT may tend to miss smaller adenomas because the median size of the adenomas detected in the CT group was significantly larger than in the AVS group (determined by CT scanning).

In patients with confirmed unilateral PA (on the basis of biochemical cure at follow up) imaging data alone would result in 1 in every 50 patients undergoing the removal of the wrong adrenal and 1 in every 3 patients missing the chance of surgery and the possibility of a cure (by being misdiagnosed as bilateral normal or bilateral abnormal). A higher number of misdiagnoses could result if patients less than 35 years of age are excluded. The overall discordance between CT and AVS results we report is highly similar to that of a systematic review (36% *versus* 38%) albeit the incidence of potential adrenalectomies on the wrong side in our study is lower (2% *versus* 4%), a difference that may be accounted for by the availability of follow-up data in all patients in our study and the inclusion of only patients with confirmed PA.[25] Despite the high level of discordance, we show in a cohort of 60 young patients (aged below 35 years) that CT scanning combined with predictors based on young age and phenotype is a reliable approach to bypass AVS as recommended by the ES guideline[6] and in agreement with a study performed in Japan.[33]

Limitations include the retrospective design and the potential for selection bias, the use of criteria for lateralization by CT that were not rigidly defined and office blood pressure measurements that were standard practice during much of the study period of patient evaluation. This may help to explain why the major differences between the CT and AVS cohorts reported herein were not defined by blood pressure measurements but by biochemical parameters.

The strengths of our study are the large cohort with patient follow-up data from diverse international centres with outcomes assessed in accordance with an internationally recognised set of criteria developed by a group of experts in the field.

**Perspectives**

Compared with AVS, a diagnosis of unilateral PA by CT results in similar clinical outcomes (blood pressure and antihypertensive medication) but decreases the likelihood of biochemical cure following treatment by adrenalectomy. Based on our data, CT based decision making is a valid strategy in young patients with PA with a marked phenotype but otherwise AVS should be considered the preferred method to differentiate unilateral from bilateral PA. Notwithstanding, it should be acknowledged that AVS is a challenging and non-standardised technique that is not available at all centres. However, the correct diagnosis and treatment of patients with unilateral forms offers a potential cure and the possibility to avoid comorbidities associated with long-term inappropriate aldosterone production.

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**Conflicts of Interests**

None

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**Novelty and Significance:**

1) What is New?

- We assessed outcomes of 761 patients treated by total unilateral adrenalectomy for unilateral primary aldosteronism with a surgical approach based on CT or AVS

- CT based management was more likely to be associated with inappropriate post-surgical aldosterone production in patients with absent clinical success

- A diagnosis by CT was associated with a decreased likelihood of complete biochemical success compared with AVS

2) What is Relevant?

CT-based management predicts a decreased likelihood of biochemical cure of unilateral primary aldosteronism after surgery compared with AVS.

**Summary**

Patients with a diagnosis of unilateral primary aldosteronism by CT scanning have unfavourable biochemical outcomes compared with a diagnosis by AVS.

**Figure Legends**

**Figure 1. Clinical and biochemical outcomes of patients stratified by surgical management decision**

Outcomes were assessed in accordance with the PASO consensus and are shown as proportions of patients (%) with absolute numbers in parenthesis for each clinical or biochemical outcome category (complete, partial or absent). A total of 233 and 235 patients had clinical and biochemical outcome data, respectively in the CT scan group and 526 patients had both clinical and biochemical outcome data in the AVS group. *p<0.001

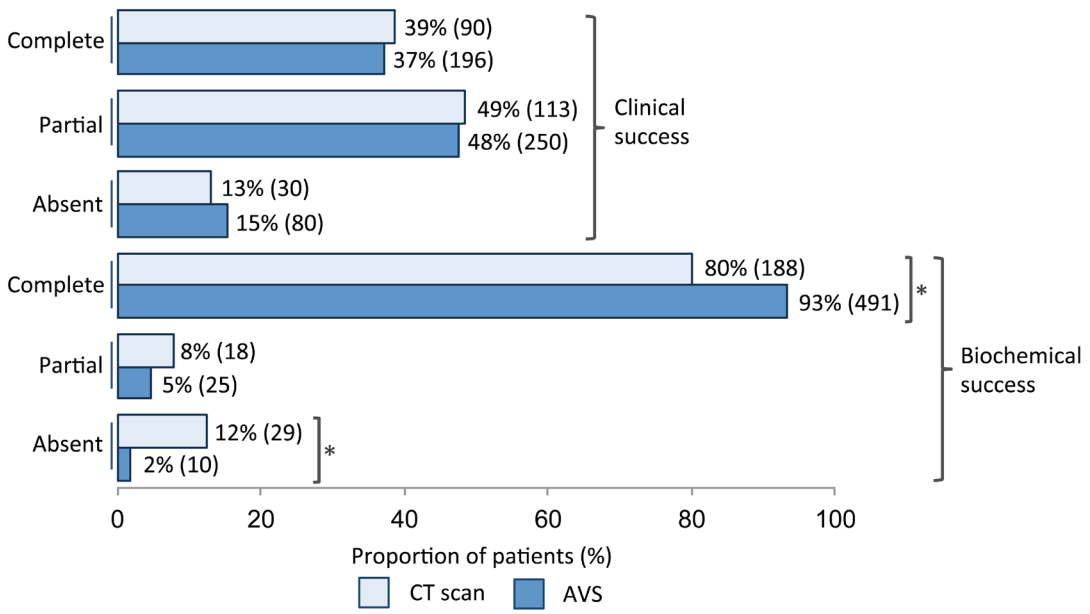


**Figure 2. Stratification of the post-surgical aldosterone-to-renin ratio by clinical outcomes and surgical management decision**

The box and whisker plot shows the median aldosterone-to-renin ratio at follow-up (thick horizontal line within bars) derived from plasma renin activities stratified for clinical outcomes (C, complete, P, partial, and A, absent clinical success) in the CT and AVS groups. The analysis included data from 136 patients

in the CT group (complete [n=55], partial [n=61] and absent [n=20] success) and from 303 patients in the AVS group (complete [n=126], partial [n=147] and absent [n=30] success).

ARR, aldosterone-to-renin ratio assessed using the plasma renin activity; AVS, adrenal venous sampling; CT, computed tomography; *p<0.001 *versus* partial and *versus* complete success in the CT group.

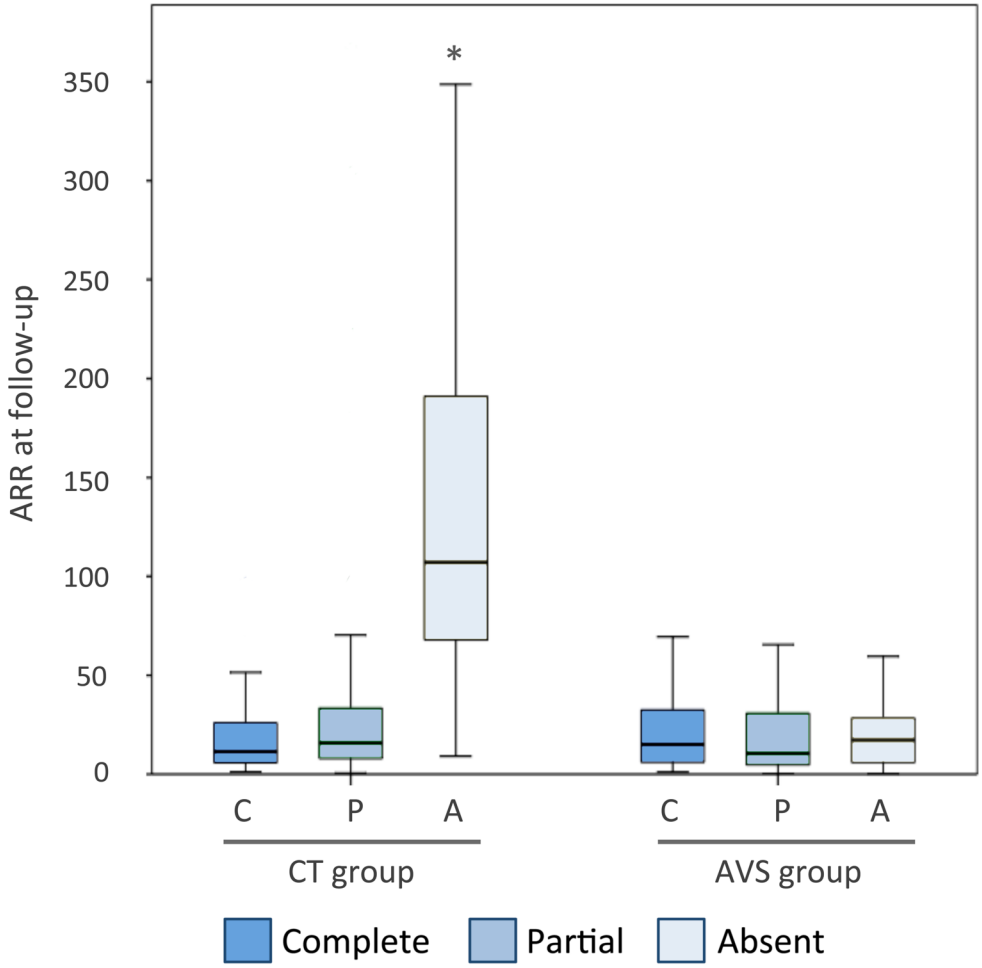


**Figure 3. Reliability of CT compared with AVS for the diagnosis of unilateral primary aldosteronism.**

485 A comparison of CT with AVS results in patients with AVS management who were biochemically cured after adrenalectomy (491 of 526 patients) indicated

discordant findings in 36% of patients (*Panel A*); there were 40 and 20 patients aged less than 35 years of age in the AVS and CT groups, respectively. The CT results indicated that 26 and 11 patients in the AVS and CT groups had a unilateral adrenal mass (> 10 mm diameter), respectively, with a normal appearing contralateral adrenal. A marked phenotype of PA at baseline (plasma aldosterone concentration > 30 ng/dL and spontaneous hypokalemia) was observed in 17 (12 complete and 5 partial clinical success) and 5 (2 complete, 2 partial clinical success and 1 with missing clinical data) of these patients, all of whom were biochemically cured by adrenalectomy (*Panel B*).

AVS, adrenal venous sampling; CT, computed tomography.

| VARIABLE | N | TOTAL | SURGICAL MANAGEMENT | | *P*-value |
|---|---|---|---|---|---|
| | | | CT | AVS | |
| **Clinical Outcome** (N = 759) | Complete | 286 (37.7) | 90 (38.6) | 196 (37.3) | 0.718 |
| | Partial | 363 (47.8) | 113 (48.5) | 250 (47.5) | 0.806 |
| | Absent | 110 (14.5) | 30 (12.9) | 80 (15.2) | 0.399 |
| **Biochemical Outcome** (N = 761) | Complete | 679 (89.2) | 188 (80.0) | 491 (93.3) | < 0.001 |
| | Partial | 43 (5.7) | 18 (7.7) | 25 (4.8) | 0.109 |
| | Absent | 39 (5.1) | 29 (12.3) | 10 (1.9) | < 0.001 |
| Age at surgery (years) | 761 | 50.4 ± 11.1 | 49.3 ± 11.3 | 50.9 ± 11.0 | 0.068 |
| Gender (Female; %) | 761 | 377 (49.5) | 132 (56.2) | 245 (46.6) | 0.014 |
| BMI (kg/m$^2$) | 761 | 27.1 ± 4.9 | 27.2 ± 4.4 | 27.1 ± 5.1 | 0.742 |
| **BASELINE PARAMETERS** | | | | | |
| Aldosterone (pmol/L) | 760 | 895.0 [590.9-1445.3] | 923.7 [635.2-1481.3] | 876.6 [569.4-1439.7] | 0.056 |
| PRA (pmol/L/min) | 460 | 2.6 [1.3-5.1] | 2.6 [2.6-4.4] | 2.6 [1.3-5.1] | 0.782 |
| ARR_PRA | 460 | 367.8 [170.2-748.7] | 419.4 [217.0-835.9] | 363.3 [158.3-708.7] | 0.072 |
| DRC (mU/L) | 301 | 4.0 [2.5-7.9] | 2.5 [2.5-3.8] | 4.9 [3.2-10.1] | < 0.001 |
| ARR_DRC | 301 | 199.8 [91.6-324.6] | 264.1 [181.4-381.4] | 153.6 [60.2-297.2] | < 0.001 |
| Lowest serum potassium (mmol/L) | 760 | 3.1 ± 0.6 | 3.2 ± 0.7 | 3.1 ± 0.6 | 0.051 |
| Systolic BP (mmHg) | 760 | 154 ± 21.4 | 159 ± 18.8 | 152 ± 22.2 | < 0.001 |
| Diastolic BP (mmHg) | 759 | 95 ± 13.4 | 99 ± 11.9 | 93 ± 13.6 | < 0.001 |
| Antihypertensive medication (DDD) | 758 | 2.7 [1.5-4.5] | 2.7 [1.7-4.3] | 2.7 [1.5-4.5] | 0.800 |
| Diabetes (yes; %) | 760 | 107 (14.1) | 29 (12.4) | 78 (14.8) | 0.373 |
| eGFR (mL/min/m$^2$) | 714 | 87 ± 23.1 | 94 ± 24.5 | 84 ± 22.0 | < 0.001 |
| 24 h Albuminuria (mg/day) | 545 | 15.0 [9.9-50.0] | 15.0 [10.0-62.8] | 15.0 [9.0-49.3] | 0.693 |

| VARIABLE | N | TOTAL | SURGICAL MANAGEMENT | | *P*-value |
|---|---|---|---|---|---|
| | | | CT | AVS | |
| LVH-Echocardiography (yes; %) | 615 | 316 (51.4) | 88 (48.4) | 228 (52.7) | 0.330 |
| Largest nodule at imaging (diameter, mm) | 761 | 14 [10.0-19.0] | 16 [11.0-22.0] | 13 [8.8-17.0] | < 0.001 |
| **FOLLOW-UP PARAMETERS** | | | | | |
| Aldosterone (pmol/L) | 760 | 241.3 [140.4-357.6] | 273.3 [141.5-438.3] | 238.6 [140.0-338.4] | 0.020 |
| PRA (pmol/L/min) | 439 | 15.4 [6.4-30.7] | 11.7 [5.7-25.6] | 19.2 [6.9-38.4] | 0.001 |
| ARR_PRA | 439 | 14.0 [5.9-33.6] | 15.1 [7.8-45.1] | 13.2 [5.4-31.0] | 0.021 |
| DRC (mU/L) | 319 | 18.8 [9.3-30.8] | 11.2 [7.2-21.9] | 22.4 [11.0-36.2] | < 0.001 |
| ARR_DRC | 319 | 13.3 [5.7-26.4] | 28.1 [16.6-42.9] | 9.4 [4.5-18.7] | < 0.001 |
| Lowest serum potassium (mmol/L) | 760 | 4.4 ± 0.5 | 4.3 ± 0.5 | 4.4 ± 0.4 | 0.356 |
| Systolic BP (mmHg) | 761 | 130 ± 14.2 | 133 ± 13.8 | 129 ± 14.3 | < 0.001 |
| Diastolic BP (mmHg) | 761 | 82 ± 9.9 | 83 ± 8.9 | 81 ± 10.3 | 0.013 |
| Antihypertensive medication (DDD) | 761 | 0.7 [0.0-2.0] | 1.0 [0.0-2.0] | 0.5 [0.0-2.3] | 0.817 |
| **POST-OPERATIVE CHANGE (BASELINE – FOLLOW UP)** | | | | | |
| Δ Systolic BP (mmHg) | 760 | 24 ± 21.2 | 26 ± 18.3 | 23 ± 22.4 | 0.140 |
| Δ Diastolic BP (mmHg) | 759 | 13 ± 13.7 | 16 ± 12.3 | 11 ± 14.2 | < 0.001 |
| Δ DDD | 758 | 1.5 [0.5-3.0] | 1.5 [0.7-2.5] | 1.5 [0.5-3.0] | 0.508 |

**Table 1. Clinical variables of patients stratified by CT or AVS based management**

The Δ post-operative changes are calculated as baseline minus follow-up as indicted. A positive value indicates a decrease and a negative value indicates an increase. BMI, body mass index; PRA, plasma renin activity; ARR, aldosterone-to-renin ratio; ARR_PRA, ARR calculated using PRA; DRC, direct renin concentration; ARR_DRC, ARR calculated using direct renin concentration; BP, blood pressure; DDD, defined daily dose (assumed average maintenance dose per day for a drug used for its main indication in adults (https://www.whocc.no/atc_ddd_index/); eGFR, estimated glomerular filtration rate; LVH, left ventricular hypertrophy.

| Variables | Clinical outcome | | Biochemical Outcome | |
|---|---|---|---|---|
| | OR (95% CI) | *P-value* | OR (95% CI) | *P-value* |
| **CT GROUP: *Complete vs. Partial + Absent (reference: Complete)*** | | | | |
| Age (per year) | 0.96 (0.92-0.99) | 0.024 | 0.99 (0.95-1.03) | 0.652 |
| Lowest serum potassium (per mmol/L) | 1.39 (0.70-2.78) | 0.347 | 2.27 (1.11-4.76) | 0.024 |
| BMI (per 1 Kg/m$^2$) | 0.99 (0.91-1.08) | 0.850 | 0.87 (0.79-0.96) | 0.007 |
| eGFR (per mL/min per 1.73m$^2$) | 1.01 (0.99-1.02) | 0.687 | 0.99 (0.98-1.01) | 0.607 |
| Sex (ref: female) | 4.37 (2.02-9.46) | < 0.001 | 1.06 (0.47-2.39) | 0.887 |
| LVH (ref: not detected) | 2.38 (1.12-5.06) | 0.025 | 1.93 (0.87-4.30) | 0.108 |
| Elevated ARR at FU (ref: not detected) | 14.81 (1.76-124.53) | 0.013 | N.A. | N.A. |
| **CT GROUP: *Complete + Partial vs. Absent (reference: Complete + Partial)*** | | | | |
| Age (per year) | 1.04 (0.98-1.11) | 0.216 | 1.00 (0.95-1.05) | 0.989 |
| Lowest serum potassium (per mmol/L) | 1.61 (0.57-4.55) | 0.370 | 3.23 (1.28-8.32) | 0.013 |
| BMI (per 1 Kg/m$^2$) | 0.95 (0.81-1.12) | 0.489 | 0.88 (0.78-0.99) | 0.044 |
| eGFR (per mL/min per 1.73m$^2$) | 1.01 (0.98-1.03) | 0.698 | 0.99 (0.98-1.02) | 0.709 |
| Sex (ref: female) | 0.88 (0.24-3.18) | 0.843 | 1.44 (0.52-3.99) | 0.483 |
| LVH (ref: not detected) | 1.00 (0.28-3.60) | 0.994 | 1.43 (0.53-3.82) | 0.480 |
| Elevated ARR at FU (ref: not detected) | 45.49 (11.63-177.93) | < 0.001 | N.A. | N.A. |
| **AVS GROUP: *Complete vs. Partial + Absent (reference: Complete)*** | | | | |
| Age (per year) | 0.95 (0.93-0.98) | < 0.001 | 0.98 (0.94-1.02) | 0.392 |
| Lowest serum potassium (per mmol/L) | 1.27 (0.85-1.85) | 0.249 | 1.52 (0.75-3.03) | 0.247 |
| BMI (per 1 Kg/m$^2$) | 0.96 (0.92-1.01) | 0.097 | 0.96 (0.89-1.03) | 0.218 |

| | | | | |
|---|---|---|---|---|
| eGFR (per mL/min per 1.73m$^2$) | 1.01 (1.00-1.02) | 0.071 | 0.99 (0.97-1.01) | 0.330 |
| Sex (ref: female) | 2.48 (1.57-3.93) | < 0.001 | 0.93 (0.41-2.14) | 0.873 |
| LVH (ref: not detected) | 1.98 (1.26-3.11) | 0.003 | 0.63 (0.28-1.43) | 0.269 |
| Elevated ARR at FU (ref: not detected) | 2.55 (0.68-9.59) | 0.166 | N.A. | N.A. |
| Basis for Surgery Decision (ref: CT scan) | N.A. | N.A. | N.A. | N.A. |
| **AVS GROUP:** ***Complete + Partial vs. Absent (reference: Complete + Partial)*** | | | | |
| Age (per year) | 0.96 (0.93-0.99) | 0.013 | 1.03 (0.96-1.11) | 0.383 |
| Lowest serum potassium (per mmol/L) | 1.30 (0.79-2.17) | 0.305 | 0.97 (0.30-3.13) | 0.956 |
| BMI (per 1 Kg/m$^2$) | 0.94 (0.89-0.99) | 0.016 | 0.89 (0.80-0.99) | 0.038 |
| eGFR (per mL/min per 1.73m$^2$) | 1.01 (0.99-1.02) | 0.427 | 1.02 (0.98-1.05) | 0.352 |
| Sex (ref: female) | 2.15 (1.15-4.01) | 0.016 | 1.76 (0.40-7.75) | 0.455 |
| LVH (ref: not detected) | 0.95 (0.54-1.69) | 0.864 | 0.62 (0.16-2.49) | 0.501 |
| Elevated ARR at FU (ref: not detected) | 1.47 (0.39-5.58) | 0.573 | N.A. | N.A. |
| Basis for Surgery Decision (ref: CT scan) | N.A. | N.A. | N.A. | N.A. |
| **AVS + CT GROUP:** ***Complete vs. Partial + Absent (reference: Complete)*** | | | | |
| Age (per year) | 0.96 (0.94-0.97) | < 0.001 | 0.99 (0.96-1.02) | 0.400 |
| Lowest serum potassium (per mmol/L) | 1.28 (0.91-1.79) | 0.157 | 1.82 (1.11-3.03) | 0.018 |
| BMI (per 1 Kg/m$^2$) | 0.97 (0.93-1.01) | 0.076 | 0.93 (0.88-0.98) | 0.007 |
| eGFR (per mL/min per 1.73m$^2$) | 1.01 (0.99-1.02) | 0.100 | 0.99 (0.98-1.01) | 0.345 |
| Sex (ref: female) | 2.90 (1.96-4.27) | < 0.001 | 0.96 (0.55-1.69) | 0.898 |
| LVH (ref: not detected) | 1.99 (1.36-2.91) | < 0.001 | 1.12 (0.64-1.95) | 0.686 |
| Elevated ARR at FU (ref: not detected) | 4.92 (1.63-14.88) | 0.005 | N.A. | N.A. |

| | | | | |
|---|---|---|---|---|
| Basis for Surgery Decision (ref: CT scan) | 1.04 (0.67-1.60) | 0.859 | 0.28 (0.16-0.50) | < 0.001 |
| **AVS + CT GROUP:** ***Complete + Partial vs. Absent (reference: Complete + Partial)*** | | | | |
| Age (per year) | 0.98 (0.95-1.01) | 0.087 | 1.01 (0.97-1.05) | 0.554 |
| Lowest serum potassium (per mmol/L) | 1.43 (0.92-2.22) | 0.114 | 2.04 (1.02-4.17) | 0.044 |
| BMI (per 1 $Kg/m^2$) | 0.93 (0.89-0.98) | 0.005 | 0.88 (0.82-0.95) | 0.002 |
| eGFR (per mL/min per 1.73$m^2$) | 1.01 (0.99-1.02) | 0.319 | 1.01 (0.99-1.02) | 0.747 |
| Sex (ref: female) | 1.81 (1.07-3.09) | 0.028 | 1.50 (0.66-3.40) | 0.327 |
| LVH (ref: not detected) | 0.94 (0.57.1.55) | 0.802 | 1.01 (0.46-2.20) | 0.999 |
| Elevated ARR at FU (ref: not detected) | 7.46 (3.35-16.63) | < 0.001 | N.A. | N.A. |
| Basis for Surgery Decision (ref: CT scan) | 1.85 (0.99-3.45) | 0.053 | 0.15 (0.06-0.36) | < 0.001 |

**Table 2. Clinical variables associated with outcomes stratified by CT- or AVS-based management decision.**

Logistic regressions identified factors associated with complete clinical and biochemical success. An odds ratio greater than 1 shows an increased odds (or likelihood) of clinical or biochemical outcome whereas an odds ratio of less than 1 means that the odds for the indicated outcome are decreased. The odds ratios for serum potassium were calculated for lowest values and therefore an odds ratio greater than 1 indicates a decreased odds and an odds ratio less than 1 means that the odds are increased. BMI, body mass index; eGFR, estimated glomerular filtration rate; LVH, left ventricular hypertrophy; ARR at FU, aldoterone-to-renin ratio at follow-up (an elevated ARR was calculated by

ARR_PRA > 65 or ARR_DRC > 102.6, with aldosterone in pmol/L, PRA in pmol/L/min and DRC mU/L); ref, reference; CT, computed tomography. NA, not applicable: an elevated ARR is a criterion of partial and absent biochemical success.