

Predictors of eGFR Decline Following Treatment for Primary Aldosteronism

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ABSTRACT

Introduction: Primary aldosteronism (PA) is the most common cause of secondary hypertension and is associated with significant cardiovascular and renal morbidity. Treatment with mineralocorticoid receptor antagonists (MRA) or adrenalectomy often leads to an early decline in estimated glomerular filtration rate (eGFR), which may be misinterpreted as renal injury rather than the correction of aldosterone-induced hyperfiltration. This study aimed to evaluate renal function changes following PA treatment and to identify predictors of eGFR decline.

Methods: A retrospective cohort study was conducted involving patients with confirmed or probable PA who attended a tertiary endocrine hypertension clinic between July 2016 and June 2023. Clinical and biochemical parameters were collected at baseline and at follow-up clinic visits after treatment. Patients were grouped according to treatment modality (MRA or adrenalectomy). Longitudinal changes in eGFR and urine albumin-to-creatinine ratio (ACR) were analysed, and multivariable regression was performed to identify independent predictors of eGFR decline.

Results: Of 421 patients, 339 (81%) received MRA therapy and 82 (19%) underwent adrenalectomy. Both groups demonstrated a modest eGFR reduction at 12-24 months, with median declines of 4 mL/min/1.73 m² and 6 mL/min/1.73 m² respectively, followed by stabilisation at long-term follow-up. Albuminuria improved significantly in both groups, with median ACR decreasing from 1.7 to 1.0 mg/mmol in the MRA group and from 2.2 to 0.7 mg/mmol after adrenalectomy (p<0.05). Among medically treated patients, age and baseline eGFR were independent predictors of post-treatment decline, while no independent predictors were found in the surgical group.

Conclusion: Treatment of PA results in a transient eGFR decline that reflects haemodynamic recovery from hyperfiltration rather than progressive renal injury. Concurrent improvements in albuminuria confirm renal benefit. Recognition of this physiological adjustment is essential to prevent inappropriate therapy discontinuation.

Keywords: Primary aldosteronism, CKD, adrenalectomy, mineralocorticoid receptor antagonists

List of Abbreviations Used:

PA – Primary Aldosteronism
BAH – Bilateral Adrenal Hyperplasia
APA – Aldosterone-Producing Adenoma
CKD – Chronic Kidney Disease
eGFR – Estimated Glomerular Filtration Rate
MRA – Mineralocorticoid Receptor Antagonist

ACEi – Angiotensin-Converting Enzyme Inhibitor
ARB – Angiotensin II Receptor Blocker
ARR – Aldosterone-to-Renin Ratio
ACR – Albumin-to-Creatinine Ratio
DMSA – Dimercaptosuccinic Acid

INTRODUCTION

Aldosterone is the principal mineralocorticoid hormone secreted by the adrenal cortex that plays a key role in regulating renal tubular sodium reabsorption and maintaining intravascular volume homeostasis (1). Primary aldosteronism (PA) is the most common endocrine cause of secondary hypertension, affecting 5-15% of patients with hypertension (2–5). It is characterised by dysregulated, renin-independent secretion of aldosterone that fails to suppress appropriately with sodium loading (6). Chronic aldosterone excess exerts deleterious effects on multiple organ systems, contributing to cardiovascular, cerebrovascular, and renal injury that extends beyond the effects of elevated blood pressure alone (7,8). Patients with PA have a 4–12-fold higher risk of cardiovascular, cerebrovascular, and renal complications than those with BP-matched essential hypertension (7–10). In recognition of the importance of treating PA, recent guidelines suggest PA screening in all adults with hypertension (11,12).

Mechanistically, aldosterone promotes renal sodium retention and extracellular volume expansion, resulting in sustained glomerular hyperfiltration and increased intraglomerular pressure (13). These haemodynamic alterations, in turn, induce podocyte injury and glomerulosclerosis, accelerating progression of chronic kidney disease (CKD) (14). Several recent studies have demonstrated that the degree of renal dysfunction seen in untreated primary aldosteronism is closely linked to renal haemodynamic adaptation to aldosterone excess and that the apparent “normal” or even elevated estimated glomerular filtration rate (eGFR) observed in untreated PA reflects maladaptive hyperfiltration rather than preserved renal function (13,14). Additionally, the hyperfiltration seen in hyperaldosteronism tends to mask the severity of underlying renal damage, making renal function challenging to interpret (15). Consequently, once aldosterone excess is corrected, either surgically or through mineralocorticoid receptor antagonist (MRA) treatment, there is a paradoxical decline in eGFR despite improvements in arterial blood pressure and reduced proteinuria (13–16).

Despite these insights, both clinicians and patients may misinterpret the early eGFR decline as evidence of treatment-induced renal injury and not the resolution of aldosterone-mediated hyperfiltration. This misconception can lead to premature discontinuation or avoidance of appropriate therapy (17), contributing to persistent aldosterone exposure with ongoing cardiovascular and renal risk.

Prior studies have been limited by small sample sizes, short follow-up durations, and incomplete biochemical characterisation, leaving uncertainty regarding the key

determinants of changes in renal function after PA treatment. Through this retrospective cohort study, we aim to identify clinical and biochemical factors associated with the degree of eGFR change after PA treatment. We hypothesise that the decrease in eGFR following either medical or surgical treatment stabilises over time and is associated with older age, longer duration of hypertension, lower baseline renal function and greater baseline albuminuria.

MATERIALS & METHODS

Study design and participants

In this retrospective cohort study, we reviewed the medical records of patients who attended the Endocrine Hypertension Clinic at Monash Health, a major tertiary health service in Victoria, Australia, from July 2016 to June 2023 for further assessment of their hypertension.

Patients were included in the final analysis if they had confirmed or highly probable PA. All patients were advised to have their screening blood test in the morning, around two hours after waking. Medications which affect aldosterone and/or renin concentration were stopped or switched to non-interfering medications, when safe to do so, for 4-6 weeks before screening (18). Highly probable PA was defined on the basis of a history of hypertension, with or without hypokalaemia, and an increased ARR ≥ 70 pmol/mU. Confirmed PA was defined by the lack of adequate aldosterone suppression following the saline suppression test. Two litres of saline was infused over 4 hours, and the diagnosis of PA was confirmed if the plasma aldosterone concentration remained ≥ 140 pmol/L (5.0 ng/dL) after a recumbent test or ≥ 170 pmol/L (6.1 ng/dL) after a seated test (19). Patients were also confirmed to have PA, without a saline suppression test, if their baseline aldosterone concentration was > 550 pmol/L, renin concentration < 2.5 mU/L, and serum potassium < 3.6 mmol/L, consistent with the 2016 Endocrine Society Clinical Practice Guideline, where the renin threshold reflects the lower limit of detection of the direct renin assay used at our institution (20).

Patients with confirmed PA underwent adrenal venous sampling to differentiate between unilateral disease, which can be cured by adrenalectomy, and bilateral disease, which can be effectively managed with targeted medical therapy (21). Medical treatment was also offered to those with unilateral PA who declined surgery after AVS.

Scanned medical records were manually assessed, for baseline data on the diagnosis of hypertension, medications and comorbidities (including coronary artery disease, stroke, atrial fibrillation and left ventricular hypertrophy). Plasma aldosterone, renin, electrolytes, renal function and blood pressure were recorded at baseline and at subsequent follow-up clinic visits extending up to 1-2 years following

treatment. Data on antihypertensive medications were only collected at baseline and at the most recent clinic visit. Patients with <12 months follow-up, baseline eGFR <15 mL/min/1.73m², or organ transplants were excluded due to management complexity and confounding medications.

Laboratory measurements

Plasma aldosterone and direct renin concentrations were measured using chemiluminescent immunoassays on a DiaSorin Liaison analyser (DiaSorin, Saluggia, Italy). For the aldosterone assay, within-run coefficients of variation (CVs) were 3.5% at 188 pmol/L and 1.8% at 798 pmol/L, with total CVs of 9.6% and 5.6%, respectively. For the direct renin assay, within-run CVs were 6.6% at 24.0 mU/L and 1.4% at 92.4 mU/L, with total CVs of 10.0% and 4.5%, respectively.

Estimated GFR was calculated based on serum creatinine levels based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. CKD stage was determined using Kidney Health Australia definitions, categorising participants into Stage 2 (eGFR 60–89 mL/min), Stage 3 (eGFR 30–59 mL/min), or Stage 4 (eGFR 15–29 mL/min) (22).

Statistical analysis

The Kolmogorov-Smirnov test was used to assess normality. Non-parametric variables were reported as median (interquartile range). Independent samples were compared using the Mann-Whitney U test, while related samples were compared using Wilcoxon matched-pair signed-rank test (for two timepoints) or Friedman's two-way analysis of variance (for more than two timepoints). Categorical variables were reported as count (percentage) and group differences were compared using the chi square test. For related samples, differences in categorical variables were compared using McNemar's test if there were two timepoints, or Cochran's Q test if there were more than two timepoints for comparison. A multivariable linear regression analysis was performed to identify predictors of change in eGFR at 12–24 months. Independent variables included age, sex, baseline blood pressure, baseline ARR, baseline eGFR, and use of ACE inhibitors or angiotensin receptor blocker. In

patients treated with MRA, the dose of MRA was also included in the regression. Changes in eGFR were calculated as the within-patient arithmetic difference between post-treatment and baseline values for each individual. Statistical analyses were performed using SPSS Statistics for Windows version 29 (IBM Corp., Armonk, NY, USA).

RESULTS

Patient demographics and clinical characteristics

Of the 873 patients who attended the Monash Health Endocrine Hypertension Clinic, 420 were excluded including 320 patients in whom PA was not identified and 100 patients who had not yet been initiated on targeted treatment. A total of 453 patients had confirmed or highly probable PA. Of these, 17 had <12 months follow-up, 13 had baseline eGFR <15 mL/min/1.73m² and two had a previous organ transplant and were therefore excluded. 421 patients were included in the final analysis. Of these, 339 patients (81%) were treated medically with MRA, while 82 patients (19%) underwent adrenalectomy for lateralised disease. Of the medically treated group, PA was confirmed via saline suppression tests in 302 (89%), while the remaining 37 patients (11%) had highly probable PA.

Table 1 shows the baseline characteristics of patients in our study. Patients were divided into two groups according to whether they were medically or surgically treated. The patients undergoing surgical treatment consisted of a significantly higher proportion of males compared to those undergoing medical treatment (67% vs 43%) and were significantly younger (mean age 51 vs 55 years). They also demonstrated higher plasma aldosterone concentrations (619 vs 453 pmol/L), and higher ARR (232 vs 120 pmol/mU). No statistically significant differences were observed in body mass index, duration of hypertension, or number of antihypertensive agents at baseline. The most common comorbidities across both surgically and medically treated patient groups were diabetes mellitus (21% and 19%, respectively), and obstructive sleep apnoea (22% and 14%, respectively). The median follow up for the medical and surgical groups were 34 and 48 months respectively.

Table 1. Baseline characteristics of medically vs surgically treated patient groups.

Patient characteristics	Treated with MRA (N=339)	Treated with adrenalectomy (N=82)
Age	55 (47, 64)	51 (42, 58)*
Male	144 (43%)	55 (67%)*
BMI	29 (26, 34)	29 (25, 31)
Duration of hypertension (years)	6 (1, 15)	10 (4, 14)
Number of antihypertensives	2 (1, 3)	2 (2, 3)
Comorbidities:		

Patient characteristics	Treated with MRA (N=339)	Treated with adrenalectomy (N=82)
Stroke	18 (5%)	6 (7%)
Myocardial infarction	15 (4%)	2 (2%)
Atrial fibrillation	27 (8%)	3 (4%)
Chronic kidney disease	21 (6%)	7 (9%)
Diabetes	64 (19%)	17 (21%)
Obstructive sleep apnoea	46 (14%)	18 (22%)
Heart failure	10 (3%)	3 (4%)
<i>Baseline medications:</i>		
MRA	57 (17%)	20 (24%)
Diuretics	61 (18%)	19 (23%)
ACE inhibitor / ARB	123 (36%)	40 (50%)
Calcium channel blocker (dihydropyridine)	107 (32%)	38 (46%)*
Calcium channel blocker (non-dihydropyridine)	79 (23%)	21 (26%)
Beta blocker	69 (20%)	15 (18%)
Prazosin	83 (25%)	23 (28%)
Moxonidine	58 (17%)	17 (21%)
Antiplatelet	25 (7%)	2 (2%)
	71 (21%)	6 (7%)*
	29 (9%)	4 (5%)
Aldosterone	453 (335, 638)	619 (411, 1240)*
Renin	3.8 (2.0, 6.0)	2.9 (1.7, 5.6)
ARR	120 (80, 187)	232 (115, 479)*
Unilateral PA	22 (8%)	82 (100%)*

* P-value < 0.05

Abbreviations: BMI = body mass index; MRA = mineralocorticoid receptor antagonist; ACE inhibitor = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; ARR = aldosterone-to-renin ratio; PA = primary aldosteronism.

Outcomes following Medical Treatment

The median follow-up duration in the medically treated group was 34 months. Systolic blood pressure decreased significantly within 1-2 years of initiating treatment, with a median reduction of 15 mmHg from baseline (Table 2). By

the most recent follow-up, blood pressure remained stable. Patients were taking a median of two antihypertensive medications at baseline (IQR 2-3), which decreased to one medication (IQR 1-3) at the most recent clinic visit ($p < 0.001$).

Table 2. Changes in blood pressure and renal function in patients treated with MRA (N=339).

	Baseline	1-2 years post treatment	Most recent
Duration of follow up (months)	N/A	21 (17, 27)	34 (21, 51)
Number of antihypertensives	2 (2, 3)	N/A	1(1, 3)
Dose of MRA	N/A	50 (25, 50)	37.5 (25, 50)
Systolic blood pressure	145 (133, 159)	130 (124, 137)*	133 (125, 142)*
Diastolic blood pressure	90 (84, 99)	83 (77, 90)*	83 (78, 90)*
Sodium	141 (139, 142)	139 (137, 141)*	139 (137, 141)*

	Baseline	1-2 years post treatment	Most recent
Potassium	4.1 (3.9, 4.4)	4.5 (4.3, 4.8)*	4.5 (4.2, 4.7)*
Renin	3.8 (2.0, 6.0)	17 (11, 35)*	15 (7.4, 32.8)*
Creatinine	71 (60, 86)	83 (69, 101)*	83 (70, 97)*
eGFR	90 (77, 90)	78 (64, 90)*	77 (61, 90)*
Change in eGFR vs baseline	N/A	-5 (-14, 0)	-4 (-14, 0)
Percentage change in eGFR (%)	N/A	-6 (-17, 0)	-6 (-18, 0)
eGFR decline of >10%	N/A	104/239 (44%)	130/297 (44%)
eGFR decline of >20%	N/A	48/239 (20%)	65/297 (22%)
Stage 2 CKD (eGFR 60-89)	122/330 (37%)	121/243 (50%)*	158/304 (52%)*
Stage 3 CKD (eGFR 30-59)	27/330 (8%)	46/243 (19%)*	62/304 (20%)*
Stage 4 CKD (eGFR 15-29)	3/330 (1%)	2/243 (1%)	3/304 (1%)
Urine ACR [^]	1.7 (0.9, 4.8)	1.0 (0.6, 2.0)*	1.0 (0.6, 2.7)*

*P<0.05 in pairwise comparison with baseline

[^]Urine ACR data was available in 132 participants (39%) at baseline, 81 participants (24%) at 12-24 months follow-up and 149 participants (44%) at the most recent clinic visit

Abbreviations: MRA = mineralocorticoid receptor antagonist; eGFR = estimated glomerular filtration rate; CKD = chronic kidney disease; ACR = albumin-to-creatinine ratio.

Among medically treated patients, age and baseline eGFR were identified as independent predictors of post-treatment eGFR decline, with coefficients of -0.195 and -0.202, respectively (Table 3). This indicates that each additional year of age and each 10 mL/min higher baseline eGFR was associated with an additional ~ 0.2 mL/min decline in eGFR post-treatment.

In the medically treated cohort, ACR data were available for 39% of participants at baseline, 24% at 12-24 months, and

44% at the most recent follow-up. The median ACR decreased from 1.7 mg/mmol at baseline to 1.0 mg/mmol at 12-24 months after commencement of MRA therapy (p<0.05) and remained 1.0 mg/mmol at the most recent follow-up.

Figure one demonstrates longitudinal changes in individual and median estimated glomerular filtration rate across both treatment groups.

Table 3. Multivariate regression to predict change in eGFR at 1-2 years in patients treated with MRA.

Characteristic	Coefficients	95.0% Confidence Interval for β		
	Beta	Lower Bound	Upper Bound	P-value
Age (per year)	-0.20	-0.45	-0.03	0.02
Female sex	-0.09	-7.2	1.44	0.19
Baseline systolic blood pressure (per 10mmHg)	-0.14	-0.27	0.06	0.20
Baseline diastolic blood pressure (per 10mmHg)	0.02	-0.24	0.28	0.90
Baseline ARR	-0.14	-0.02	0.001	0.07
Baseline eGFR (per 10 mL/min/1.73m ²)	-0.20	-0.40	-0.05	0.01
Use of ACEiARB	-0.11	-7.94	0.94	0.12
MRA dose (per 25 mg)	-0.03	-0.10	0.07	0.73

Abbreviations: ARR = aldosterone-to-renin ratio; eGFR = estimated glomerular filtration rate; ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; MRA = mineralocorticoid receptor antagonist.

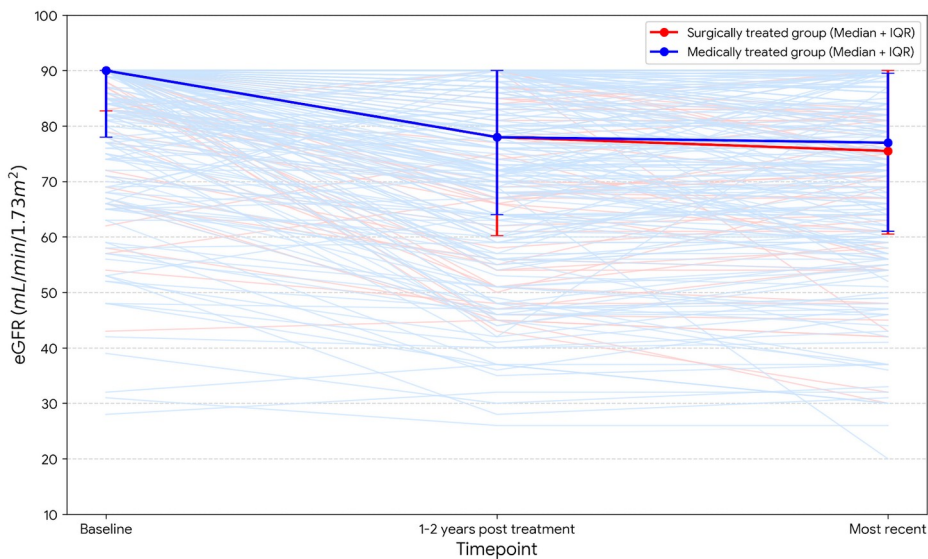


Figure 1. Longitudinal changes in individual and median estimated glomerular filtration rate (eGFR) with interquartile ranges following surgical vs medical treatment for primary aldosteronism. The surgically treated group is denoted in red, and the medically treated group is denoted in blue. “Most recent” represents the final clinical follow-up recorded for each participant, which was a median of 34 months for the medically treated group and 48 months for the surgically treated group. eGFR is measured in mL/min/1.73m².

Outcomes following Surgical Treatment

The median follow-up duration in the surgically treated group was 48 months. Systolic blood pressure decreased

significantly within 1-2 years of initiating treatment, with a median reduction of 21 mmHg from baseline (Table 4). By the most recent follow-up, blood pressure remained stable.

Table 4. Changes in blood pressure and renal function in patients treated with adrenalectomy (N= 82).

	Baseline	1-2 years post treatment	Most recent
Duration of follow up (months)	N/A	29 (23, 35)	48 (27, 64)
Number of antihypertensives	2 (2, 3)	N/A	1 (1, 3)
Systolic blood pressure	151 (142,164)	130 (125, 141)*	133 (124, 140)*
Diastolic blood pressure	91 (86, 100)	83 (79, 90)*	84 (78, 91)*
Sodium	141 (139,143)	140 (138, 141)*	139 (137, 140)*
Potassium	3.9 (3.5, 4.2)	4.6 (4.4, 4.8)*	4.5 (4.3, 4.8)*
Renin	2.9 (1.7, 5.6)	20 (9.5, 39.4)*	16 (8.9, 32)*
Creatinine	75 (62, 95)	92 (74, 106)*	95 (78, 117)*
eGFR	90 (78, 90)	78 (57, 90)*	74 (56, 90)*
Change in eGFR	N/A	-6 (-19, 0)	-7 (-18, 0)
Percentage change in eGFR	N/A	-8 (-22, 0)	-10 (-21, 0)
eGFR decline of >10%	N/A	33/67 (49%)	37/74 (50%)
eGFR decline of >20%	N/A	19/67 (28%)	19/74 (26%)
Stage 2 CKD (eGFR 60-89)	30/82 (37%)	27/67 (40%)	32/74 (43%)
Stage 3 CKD (eGFR 30-59)	6/82 (7%)	17/67 (25%)*	21/74 (28%)*
Stage 4 CKD (eGFR 15-29)	1/82 (1%)	1/67 (2%)	0 (0%)
Urine ACR [^]	2.2 (0.9, 10)	0.7 (0.4, 1.1)*	1.0 (0.6, 3.0)*

*P<0.05 compared to baseline

^aUrine ACR data was only available in 35 participants (43%) at baseline, 21 participants (26%) at 12-24 months follow-up and 43 participants (52%) at the most recent clinic visit

Abbreviations: eGFR = estimated glomerular filtration rate; CKD = chronic kidney disease; ACR = albumin-to-creatinine ratio.

The median baseline eGFR in the surgical cohort was 90 mL/min/1.73 m², with a median within-patient decline of 6 mL/min/1.73 m² (8%) at 12–24 months postoperatively and 7 mL/min/1.73 m² (10%) at the most recent follow-up.

At baseline, 37% of patients were classified as Stage 2 CKD, 7% as Stage 3, and 1% as Stage 4. The prevalence of Stage 3 CKD significantly increased to 25% at 12-24 months and 28% at the most recent follow-up, with no significant changes observed in other CKD categories.

Consistent with the medically treated group, there were no significant changes in the proportions of patients experiencing >10% or >20% declines in eGFR over time.

In the surgical group, urine ACR data was available in 43% of participants at baseline, 26% at 12-24 months follow-up and 52% at the most recent follow-up. The median ACR decreased from 2.2 mg/mmol at baseline to 0.7 mg/mmol at 12-24 months ($p < 0.05$), and stabilising at 1.0 mg/mmol at the most recent follow-up.

No significant difference in absolute or percentage eGFR change was observed between the medically and surgically treated groups at 12-24 months or the latest follow-up. No independent predictors of eGFR decline were identified in the surgically treated cohort.

DISCUSSION

PA is known to be associated with renal injury via aldosterone mediated hyperfiltration and stimulation of profibrotic and proinflammatory pathways (14,23). These effects accelerate renal structural damage despite apparently normal kidney function. In our previous study, we found that the screening rate for PA in patients with CKD was low (24). This is particularly significant due to the cardiovascular and renal sequelae associated with untreated disease. To date, studies examining changes in renal function following targeted PA treatment have been limited by short follow-up durations, inconsistent definitions of renal outcomes, and limited evaluation of microalbuminuria. In our study of 421 patients, rigorous diagnostic confirmation testing was performed, and patients were stratified by treatment modality. Renal outcomes following PA treatment were evaluated over a median follow-up period of 34 months for the medically treated group and 48 months for the surgically treated group. To our knowledge, this is the first study to evaluate longitudinal renal outcomes following PA treatment in an Australian population.

In our study, both medically and surgically treated cohorts demonstrated a modest early decline in eGFR after targeted PA therapy. The median reduction at 12-24 months was 6

mL/min/1.73 m² (8%) following adrenalectomy and 5 mL/min/1.73 m² (6%) in the medically treated group. Importantly, eGFR values subsequently stabilised, with no further decline after an extended follow-up. This temporal pattern, an initial fall followed by a plateau, strongly supports a haemodynamic rather than a structural basis for the fall in eGFR. Resolution of aldosterone-driven hyperfiltration likely restores intraglomerular pressure to physiological levels, resulting in an apparent “loss” of filtration capacity that actually reflects recovery from chronic glomerular hyperfiltration (7,13,14,16,25,26). The magnitude of eGFR decline observed in our cohort is comparable to previous reports, where early reductions of 5–10% are typical and usually self-limiting (27,28). Notably, a 2022 meta-analysis of 21 studies and 1,522 patients found the mean decline in eGFR post PA treatment to be 12.2 mL/min/1.73 m² in the adrenalectomy group and 8.4 mL/min/1.73 m² in the medically treated group (29).

The concurrent improvement in albuminuria across both treatment arms reinforces this interpretation. Median ACR decreased following therapy, from 1.7 to 1.0 mg/mmol in the MRA group and 2.2 to 0.7 mg/mmol after adrenalectomy, remaining low at long-term follow-up. The parallel between ACR reduction and eGFR stabilisation supports the hypothesis that the early functional decline in eGFR is accompanied by structural and endothelial improvement at the glomerular level (30) with improved renal vascular resistance after aldosterone suppression (31).

Prior studies of biochemical and clinical predictors of post-treatment eGFR decline have found mixed results. In a cohort of 213 patients, Iwakura et al. identified higher baseline aldosterone-to-renin ratios, lower pretreatment eGFR, and older age as independent predictors of greater eGFR decline following either adrenalectomy or MRA therapy (28). In contrast, Kobayashi et al. and Kim et al. demonstrated that a larger acute eGFR drop occurred in patients with higher baseline filtration rates (27,32). Our data similarly showed that patients with higher baseline eGFRs experienced proportionally greater declines after therapy, supporting the concept that the fall in eGFR reflects reversal of aldosterone-induced hyperfiltration. Conversely, those with pre-existing CKD or lower baseline eGFR demonstrated a less steep decline in eGFR but were more likely to meet criteria for CKD progression during follow-up due to their low baseline eGFR. These findings reinforce the conclusion that post-treatment eGFR trajectory is influenced not only by the severity of hyperaldosteronism, but also by the degree of kidney damage caused by both aldosterone excess and hyperfiltration. This association has also been reported by Kuo et al. (33). More recent studies, such as

Nakano et al. have further associated older age and longer duration of hypertension with more pronounced declines in post treatment eGFR (34).

Previous studies have found mixed results for the ARR as a predictor of renal function decline. Tanase-Nakao et al found ARR to be a significant predictor for the development of CKD post-treatment (35), while Kim et. al. reported that the ARR was not a significant predictor (32). However, in our study, the ARR was not significantly associated with the development of CKD. The absence of a significant association between ARR and post-treatment renal outcomes in our cohort may reflect the relatively mild degree of biochemical disease severity, as evidenced by only modest baseline hypokalaemia, which may have attenuated the haemodynamic signal that ARR captures. Furthermore, early identification and treatment through a dedicated tertiary endocrine hypertension clinic may have limited the degree of aldosterone-mediated renal injury accrued prior to diagnosis, reducing the discriminatory value of ARR as a predictor of subsequent renal decline.

The relationship between pre-treatment hypokalaemia and post-treatment renal impairment similarly remains a subject of conflicting evidence. While some studies, particularly those with cohorts exhibiting severe hypokalaemia and significant aldosterone excess, have identified low serum potassium as an independent predictor of eGFR decline (28,36), others, including ours, failed to demonstrate this association (25,35). This discrepancy likely stems from several factors. Firstly, hypokalaemia may serve as a surrogate marker for the severity of aldosterone-driven glomerular hyperfiltration (27,37); thus, its predictive value is most pronounced in cohorts with severe PA. Additionally, chronic potassium depletion may lead to hypokalaemic nephropathy, characterized by impaired proximal tubular reabsorption and albuminuria (38). However, in the setting of advanced renal damage, impaired potassium excretion may paradoxically "normalise" serum potassium levels, masking the link between hypokalaemia and renal outcomes (25,39). In our cohort, where potassium levels were generally only mildly reduced, this haemodynamic signal may have been less dominant. Therefore, while hypokalaemia is often considered to be a hallmark of disease severity in PA, its presence alone may not independently predict renal function decline, especially in patients with pre-existing CKD.

These findings have several clinical implications. First, Clinicians should be reassured that an initial acute eGFR decline following MRA therapy or adrenalectomy is common and typically stabilises. This early fall most likely represents a haemodynamic recalibration rather than a loss of nephron function. Our data showed similar reductions in eGFR following medical and surgical treatment, with median declines of 6% and 8% respectively, supporting the

continuation of MRA therapy within this range of change. However, a severe acute drop or a gradual, progressive decline beyond the initial 1-2 year stabilisation period should prompt evaluation for concurrent or alternative causes of renal impairment. Educating both patients and clinicians about the expected eGFR trajectory can help prevent inappropriate discontinuation or dose reduction of MRA therapy in the management of PA.

The strengths of this study lie in its relatively large, well-characterised cohort of patients with primary aldosteronism who underwent robust diagnostic tests and were longitudinally followed at a dedicated tertiary endocrine hypertension clinic. The inclusion of both medically and surgically treated patients allows for a balanced comparison of therapeutic modalities, providing valuable real-world insight into renal outcomes across treatment strategies. The primary limitation of our study is its retrospective nature, which may introduce potential biases in data collection, including incomplete biochemical and urine albumin data for some patients. Additionally, given that additional follow-up and laboratory monitoring intervals were guided by clinical discretion rather than a fixed protocol, inter-individual variability in timing may have influenced longitudinal comparisons.

CONCLUSION

In conclusion, this study demonstrates that treatment of primary aldosteronism, whether through MRA or adrenalectomy, results in a <10% decline in eGFR that subsequently stabilises. This may reflect resolution of aldosterone-induced hyperfiltration rather than progressive renal impairment. The concurrent improvement in albuminuria underscores the renal protective effects of targeted therapy. Baseline eGFR and age emerged as potential predictors of post-treatment decline, highlighting the importance of individualised monitoring and early diagnosis. Clinicians should recognise this transient eGFR reduction as a likely physiological recalibration and not a marker of new injury that requires MRA dose reduction or cessation. Early identification and appropriate treatment remain essential to prevent long-term cardiovascular and renal sequelae of PA.

DECLARATIONS

Disclosures

The authors declare no conflicts of interest.

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