U-shaped relationship between left ventricular mass index and estimated glomerular filtration rate in patients with primary aldosteronism

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ABSTRACT

Estimated glomerular filtration rate (eGFR) is an important topic in patients with primary aldosteronism (PA). However, the relationship between left ventricular structure and eGFR is unclear. We conducted a prospective, observational, and cross-sectional study to analyze 168 patients with PA and 168 propensity score-matched patients with essential hypertension (EH) as the control group, matched by age, gender, and systolic blood pressure. In the patients with PA, the eGFR was not correlated with left ventricular mass index (LVMI; r=−0.065, p=0.404), while in the patients with EH, the eGFR was negatively correlated with LVMI (r=−0.309, p<0.001). To test whether eGFR had a non-linear relationship with LVMI among the patients with PA, we stratified the patients with PA according to the tertile of eGFR (low, medium, and high tertile). The medium tertile of patients had a significantly lower LVMI than those in the other two tertiles (LVMI: 143.5±41.6, 120.5±40.5, and 133.1±34.3 g/m^2, from the lowest to highest tertile of eGFR; analysis of covariance p=0.032). The medium tertile of eGFR is associated with lowest LVMI. Patients with PA with high and low eGFR were associated with higher LVMI. The findings implied that the reasons for an increased LVMI in patients with PA may be different to those in patients with EH.

Significance of this study

What is already known about this subject?

- The reported prevalence of primary aldosteronism (PA) in the general hypertensive population varies widely, ranging from 1% to 29.8% and PA is characterized by an excessive production of aldosterone.
- Patients with PA have a higher risk of end-organ damage, including stroke, coronary artery disease, heart failure, and atrial fibrillation compared with essential hypertension (EH).
- Negative linear relationships between estimated glomerular filtration rate (eGFR) and left ventricular mass (LVM) have been demonstrated in patients with EH.

What are the new findings?

- The relationship between eGFR and LVM index was not linear in patients with PA.
- The primary aldosteronism patients in the median tertile of eGFR had a significantly lower LVM index than those in the other two tertiles.
- The causes of increased LVM index in patients with PA may be different to those in patients with EH.

How might these results change the focus of research or clinical practice?

- There is a U-shaped relationship between LVM index and eGFR in patients with PA, which is distinctly different to the negative linear relationship in patients with EH.

INTRODUCTION

High blood pressure has been associated with increased rates of coronary heart disease, stroke, and renal impairment.[1] A systematic analysis of the Global Burden of Disease Study in 2010 showed that high blood pressure was the leading cause of mortality worldwide.[2] The most common cause of secondary hypertension is primary aldosteronism (PA). The reported prevalence of PA in the general hypertensive population varies widely, ranging from 1% to 29.8%.[3–6] A systematic review data showed greatly variable prevalence and high heterogeneity between studies.[7] The heterogeneous results of these studies have been associated with geographic differences, patient selection, healthcare setting and variability in screening tests and diagnostic methods.[8] A relatively large and careful study published after that systematic review found a prevalence of 5.9%.[9]

PA is caused by the excessive secretion of aldosterone from the adrenal gland, which can induce cardiac fibrosis and left ventricular

hypertrophy (LVH).[10 11] A recent systematic review and meta-analysis showed that PA is associated with increased rates of stroke, coronary artery disease, heart failure, and atrial fibrillation compared with essential hypertension (EH).[12]

Hypertension is the second leading cause of end-stage renal disease, accounting for 34% of all cases of ESRD in the USA.[13] In community samples, negative linear relationships between estimated glomerular filtration rate (eGFR) and left ventricular mass (LVM) have been demonstrated, showing an association between a lower eGFR and a higher LVM.[14 15] However, eGFR is also an important issue in patients with PA, who have relative hyperfiltration compared with patients with EH.[16 17] Knowledge on the relationship between left ventricular structure and eGFR in patients with PA with hypertension is still limited. Therefore, the aim of this study was to investigate the association between eGFR and LVM in patients with PA.

METHODS

Patients

This prospective observational study included 168 patients diagnosed with PA according to the guidelines of the Taiwan Primary Aldosteronism Investigation (TAIPAI) group[18 19] from October 2006 to March 2010. All of the patients were registered in the TAIPAI database, which includes data from one medical center (NTUH, National Taiwan University Hospital), Yun-Lin Branch of NTUH, and two cooperating hospitals (Far-Eastern Memorial Hospital and Tao-Yuan General Hospital).[20–24] The study was approved by the institutional review board of our institution. Informed Consent has been obtained from each patient after full explanation of the purpose and nature of all procedures used.

In addition, another 168 propensity score-matched patients with EH were enrolled for comparison. Propensity scores were used to match by age, gender, and systolic blood pressure (SBP). Population characteristics and medications were cautiously reviewed. Laboratory data were checked at the first evaluation of the patients at NTUH. Body mass index (BMI) was obtained and eGFR was calculated according to the Chinese Modification of Diet in Renal Disease (MDRD) Study equation (eGFR=186.0 • (serum creatinine)$^{-1.154}$ • age$^{-0.203}$ • (0.742 if female)).[25 26]

Antihypertensive medications were discontinued for more than 21 days before measuring plasma aldosterone concentration (PAC) and plasma renin activity (PRA) levels. Markedly high blood pressure was treated by diltiazem and/or doxazosin if required. A commercially available radioimmune assay kit (Aldosterone Maia Kit; Adaltis Italia, Bologna, Italy) was used to measure PAC. A commercially available radioimmune assay kit (Cisbio, Bedford, Massachusetts, USA) was used as the generation of angiotensin-I in vitro to measure PRA.

Diagnostic criteria of the subtypes of PA

The 'modified four-corner approach' was used to validate the diagnosis of aldosterone-producing adenoma. The 'modified four-corner approach' meets all of the following criteria:[20 21 27 28] (1) evidence of autonomous excess aldosterone production based on an aldosterone-renin ratio (ARR) >35 or urine ≥12 µg/24 hours, a TAIPAI score >60%, and a postsaline loading PAC >10 ng/dL. TAIPAI score is the probability of PA which was estimated by PAC, PRA, ARR, BMI, gender, serum potassium, and eGFR;[17] (2) adrenal vein sampling (AVS) or dexamethasone suppression adrenocortical scintigraphy (NP-59 SPECT/CT) revealed lateralization of aldosterone secretion;[29] (3) CT revealed adenoma; and (4) an adrenalectomy proved adenoma pathologically if performed, and cure or improvement of hypertension without antihypertensive agents or improved potassium, PAC, and PRA as previously described.[17] Idiopathic hyperaldosteronism was defined by the four criteria: (1) evidence of autonomous excess aldosterone production based on an ARR >35 or urine ≥12 µg/24 hours, a TAIPAI score >60%, and a postsaline loading PAC >10 ng/dL; (2) AVS or NP-59 SPECT/CT revealed non-lateralization of aldosterone secretion;[29] (3) CT revealed bilateral diffuse enlargement of adrenal gland; and/or (4) pathology studies revealed diffuse cell hyperplasia.

Echocardiography

An echocardiographic ultrasonic system (Hewlett-Packard Sonos 5500 ultrasound system or IE33, Philips; Andover, Massachusetts, USA) was used for the evaluations. Echocardiography demonstrated two-dimensional, M-mode, and Doppler ultrasound recordings. The chamber size and shape including dimensions of left ventricular, ventricular septum, posterior wall, and left atrial diameter and left ventricular ejection fraction by M-mode were all measured via the parasternal long-axis view according to the American Society of Echocardiography.

The method of Devereux *et al*[30] was used to calculate the left ventricular mass index (LVMI) and LVH was defined as LVMI ≥134 gm^{-2} in men and ≥110 gm^{-2} in women.[31] End-diastolic relative wall thickness (RWT) as one additional index of LV concentric geometry provides the further classification of increased LVM. RWT is defined as the ratio of posterior wall thickness to one half of the LV end-diastolic diameter. In patients with LVH, a RWT>0.42 has been used as a threshold of concentric LVH, and ≤0.42 as eccentric LVH. In patients with normal LVMI, a RWT>0.42 has been used as a threshold of concentric remodeling, and ≤0.42 as normal geometry.[32] The Teichholz method[33] was used to calculate LV end-diastolic and end-systolic volumes.

An equation developed previously was used to estimate the theoretical value of predicted LVM: predicted LVM (pLVM)=55.37+66.4 × height (m$^{2.7}$)+0.64 × stroke work (SW) – 18.07 × gender (male=1 and female=2). SW was defined as SBP (in mm Hg) × stroke volume × 0.0144.[34] Inappropriate LVM was defined as an excess of >35% from the predicted value.[34] Interobserver and intraobserver findings are available in our previous echocardiography study.[35]

Statistical analysis

Descriptive statistics were represented as mean±SD. Continuous data between the two groups were compared using the Student's test. Discrete data were compared using the χ^2 test or Fisher's exact test. PRA and ARR data were log-transformed due to non-normality, which was tested using the Kolmogorov-Smirnov test.

Propensity score methodology can be used to observational studies and is only to match covariates, not outcomes

Table 1 Baseline characteristics of the study population

Clinical characteristics	PA (n=168)	EH (n=168)	P value
Age, years	50.3±11.8	50.9±14.3	0.676
Sex (male)	75 (44.6)	80 (47.6)	0.584
Body weight, kg	66.4±13.3	68.1±14.2	0.249
Body height, cm	161.2±8.4	163.1±9.7	0.047
Body mass index, kg/m^2	25.4±3.7	25.4±3.9	0.930
SBP, mm Hg	149.6±20.2	147.8±19.7	0.424
DBP, mm Hg	89.7±12.2	87.0±13.2	0.052
MBP, mm Hg	109.6±12.8	107.3±13.9	0.104
Estimate duration of hypertension, years	7.7±8.0	7.7±7.4	0.938
Laboratory variables			
Creatinine, mg/dL	1.00±0.56	1.08±0.80	0.299
eGFR, mL/min/1.73 m^2	81.3±21.7	80.5±24.6	0.821
Potassium, mmol/L	3.42±0.73	4.14±0.43	<0.001
PAC, ng/dL	47.2±34.0	36.5±22.7	0.001
PRA, ng/mL/hour	0.95±2.16	5.22±8.62	<0.001
Hypertension medication			
CCB	107	46	<0.001
ACEI/ARB	43	36	0.305
Spironolactone	74	5	<0.001
α-blocker	50	3	<0.001
β-blocker	85	15	<0.001

Values are expressed as mean±SD or number (percentage).
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; MBP, mean blood pressure; PAC, plasma aldosterone concentration; PRA, plasma renin activity;SBP, systolic blood pressure.

Table 2 Baseline echocardiographic parameters of the study population

Echocardiographic parameters	PA (n=168)	EH (n=168)	P value
IVST, mm	11.7±2.4	11.4±2.5	0.233
LVPWT, mm	11.0±1.9	10.8±1.9	0.224
LVEDD, mm	46.0±5.3	46.2±5.0	0.815
LVESD, mm	27.7±4.6	28.0±5.3	0.603
LVEDV	99.3±25.8	99.7±25.5	0.878
LVESV	30.1±12.9	31.3±14.9	0.454
LVEF, %	69.5±7.9	68.8±10.2	0.479
LVH	99 (59)	40 (24)	<0.001
Relative wall thickness	0.50±0.11	0.48±0.10	0.169
Concentric LVH	78 (46)	36 (21)	<0.001
Eccentric LVH	21 (13)	4 (2)	<0.001
Concentric remodeling	46 (27)	90 (54)	<0.001
Normal geometry	23 (14)	38 (23)	0.023
LVM, g	228.9±78.7	192.8±75.2	<0.001
LVMI, g/m^2	132.4±39.8	110.7±39.0	<0.001
Predicted LV mass, g	147.5±35.5	146.4±36.1	0.771
Observed/predicted LVM (%)	156.1±43.9	125.5±59.4	<0.001
Inappropriate LVM	110 (65)	51 (30)	<0.001

Value are mean±SEM.
IVST, interventricular septal thickness; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVESV, left ventricular end-systolic volume; LVH, ventricular hypertrophy; LVM, left ventricular mass; LVMI, left ventricular mass index; LVPWT, left ventricular posterior wall thickness.

to identify patients with similar basic characteristics.[36] First, propensity scores were used to match age, gender, and SBP between the two groups. Pearson's correlation test, linear regression analysis, and quadratic regression analysis were used to analyze the association between eGFR and LV structural parameters in the patients with PA and those with EH. To test the nonlinear relationship between eGFR and LVMI in the patients with PA, we stratified the patients into tertiles according to the eGFR level (low, medium, and high tertiles). An analysis of covariance (ANCOVA) was performed to test the effect of eGFR tertile on LVMI after adjusting age, gender, mean blood pressure, and duration of hypertension in patients with PA. Another ANCOVA was used to test the effect of PA or EH groups and eGFR tertiles on LVMI. We also tested the interaction between PA or EH groups and eGFR tertile. Kruskal-Wallis with Dunn's analysis was used for post-hoc analysis for eGFR tertiles separately in the PA and EH groups. Statistical analyses were performed using SPSS V.22.0 for Windows (SPSS, Chicago, Illinois, USA) and plot drawing was performed using Graphpad Prism V.7.0.

RESULTS

Patient characteristics

One hundred and sixty-eight patients with PA were enrolled, and another 168 patients with EH with propensity-score matched by age, gender and SBP were also enrolled. The clinical data are shown in table 1. The mean age was 50.3±11.8 years in the PA group and 50.9±14.3 years in the EH group. The serum creatinine level was similar between the two groups. The patients with PA had a higher PAC, lower PRA, and significantly lower serum potassium level than the patients with EH (p<0.001). The patients with PA also had a lower body height than the patients with EH (p=0.047). With regard to medication usage, the percentage of patients with PA using antihypertensive drugs was higher than that of the patients with EH, especially spironolactone and alpha-blockers.

Echocardiographic data

The echocardiographic data are shown in table 2. The patients with PA had a significantly higher LVMI (132.4±39.8 gm^{-2}) than the patients with EH (110.7±39.0 gm^{-2}) (p<0.001). Significantly more patients with PA had LVH than the patients with EH (50% vs 24%; p<0.001). The LV geometry of the patients with PA was more in concentric LVH (46%), whereas it was more in concentric remodeling (54%) in the patients with EH. Significantly more patients with PA had inappropriate LVM than the patients with EH (65% vs 30%; p=0.024).

Relationship between LVMI and eGFR

The correlations between eGFR and LV structural parameters among the patients with PA and EH are shown in table 3. In the patients with PA, the eGFR was not correlated with LVMI (r=−0.065, p=0.404) or inappropriate LVMI (r=0.061, p=0.433). However, in the patients with EH,

Table 3 The correlations between eGFR and LV structural parameters among (1) patients with primary aldosteronism or (2) patients with essential hypertension

		Primary aldosteronism		Essential hypertension	
		Correlation coefficient	P value	Correlation coefficient	P value
LVMI	eGFR	−0.065	0.404	−0.309	<0.001
Inappropriate LVMI	eGFR	0.061	0.433	−0.206	0.008

eGFR, estimated glomerular filtration rate; LVMI, left ventricular mass index.

the eGFR was negatively correlated with LVMI (r=−0.309, p<0.001) and inappropriate LVMI (r=−0.206, p=0.008).

In patients with EH, a linear regression analysis suggested a decrease of 0.489 LVMI units for each unit increase in eGFR (R=−0.309, p<0.001, figure 1B) and a quadratic regression analysis suggested a better model fit for the relationship between eGFR and LVMI (R=−0.364, p<0.001, figure 1B). However, there were five very high levels of LVMI at low eGFR tertile. This could suggest a better nonlinear relationship. In patients with PA, a linear regression analysis demonstrated there was no change of LVMI in the response of eGFR (p=0.404, figure 1A) and a quadratic regression analysis suggested a better model fit for the relationship between eGFR and LVMI (R=−0.215, p=0.020, figure 1A). This implied the relationship between eGFR and LVMI in patients with PA was nonlinear.

To test whether eGFR had a nonlinear relationship with LVMI among the patients with PA, we stratified the patients with PA according to the tertile of eGFR (low, medium, and high tertiles). We plotted LVMI according to eGFR tertile (figure 2A for the patients with PA; figure 2B for the patients with EH). The LVMI values of the PA group in the low, medium, and high eGFR tertiles were 143.5±41.6, 120.5±40.5, and 133.1±34.3 gm^{-2}, respectively. The results revealed that the patients with PA in the medium eGFR tertile had a lower LVMI compared with the high and low eGFR tertiles. Among the PA group, an ANCOVA showed a significant difference in LVMI between the eGFR tertiles after adjusting for covariates (p=0.032) (table 4). In order to test the effect of PA compared with EH in all patients with hypertension, an ANCOVA for all patients showed a significant difference in LVMI between patients with PA and EH after adjusting for covariates (p<0.001, table 4), which implied the effect of aldosterone played a more important role on LVMI in patients with PA than patients with EH. And there was no interaction between eGFR tertiles and both groups (p=0.449, table 4). In patients with PA, posthoc analysis with Kruskal-Wallis with Dunn's test revealed a significant difference between the eGFR tertiles (p=0.008), between the low and medium tertile (p=0.003) and medium and high tertiles (p=0.033) (figure 2A). In patients with EH, posthoc analysis with Kruskal-Wallis with Dunn's test revealed a significant difference between the eGFR tertiles (p=0.001), medium and high tertiles (p=0.033), and a significant trend between the low and medium tertile (p=0.053) (figure 2B).

DISCUSSION

To the best of our knowledge, this is the first study with a large sample size to investigate the relationship between LVMI and eGFR in patients with PA. Our results demonstrated that in the patients with PA, the medium tertile of eGFR was associated with a lower LVMI compared with the low and high tertiles of eGFR, and that there was a U-shaped relationship between eGFR and LVMI in the patients with PA. We also showed that in hospital samples, the propensity scored-matched patients with EH had a significantly and negatively linear relationship. These results are similar to previous studies in community samples.[14 15]

In the Framingham heart study, hypertension was the most common cause of LVH.[37] However, it has been shown that, apart from pressure overload, aldosterone is also an important cause of LVH.[38 39] Mastumura *et al* reported

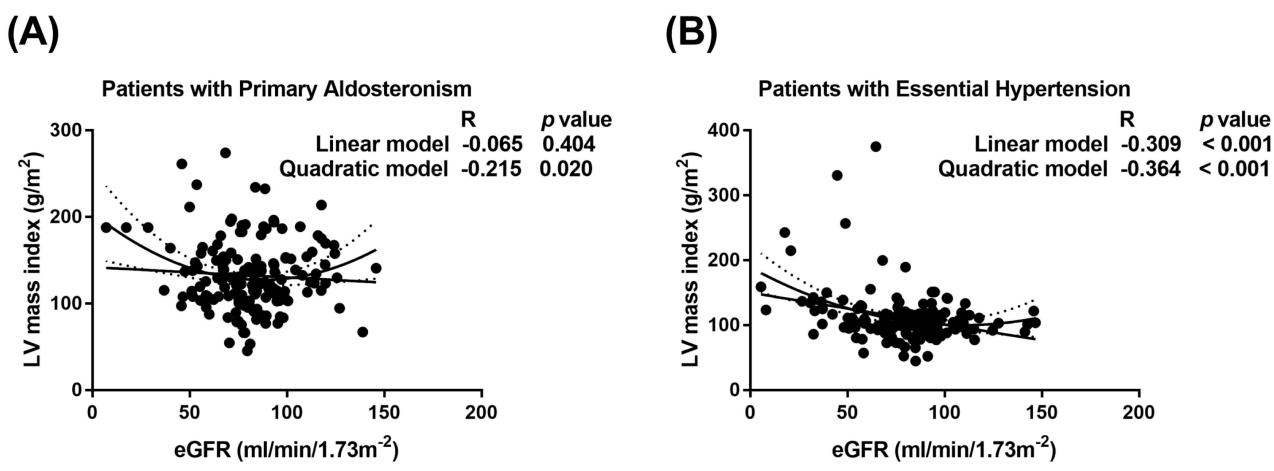

Figure 1 Linear and quadratic regression analysis of LV mass index and eGFR among patients with primary aldosteronism (A) or essential hypertension (B). eGFR, estimated glomerular filtration rate; LV, left ventricle.

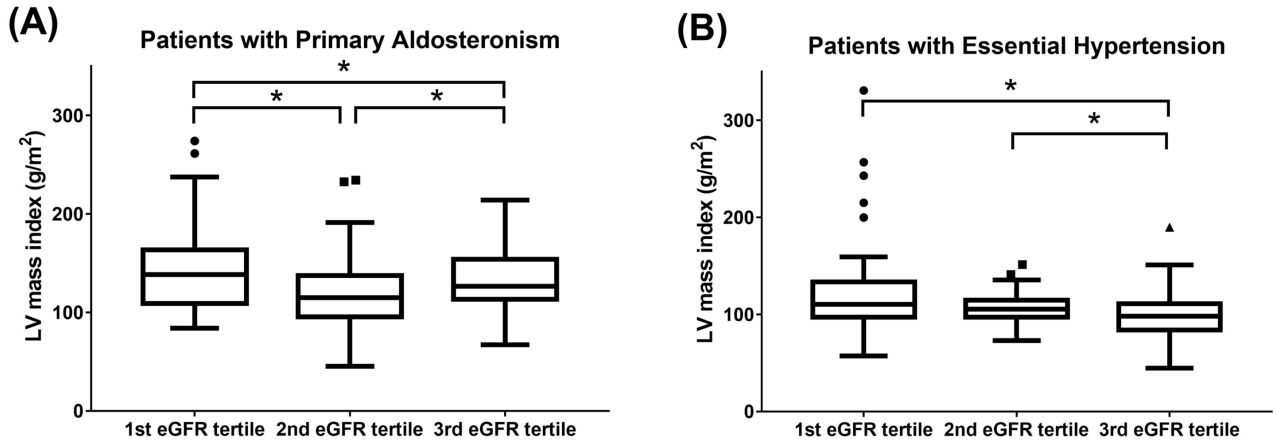

Figure 2 Box plots of LV mass index by eGFR tertiles among patients with primary aldosteronism (A) or essential hypertension (B). The thick horizontal line represents the median LV mass index, the box represents IQR, whiskers represent (first quartile −1.5IQR, third quartile +1.5IQR), and dots represent outlying observations. *P<0.05 in posthoc analysis. eGFR, estimated glomerular filtration rate; LV, left ventricle.

that patients with PA had the highest LVMI adjusted by age, gender, mean 24 hours SBP, mean 24 hours pulse rate, BMI, and duration of hypertension compared with patients with EH and renovascular hypertension.[11] High aldosterone levels may induce cardiac fibrosis, leading to LVH in patients with PA.[10 11] Muiesan *et al* reported that patients with PA had a higher prevalence of inappropriate LVM than patients with matched EH.[40] This suggests that aldosterone contributes to the increase in LVM. We also found a greater prevalence of inappropriate LVM in our patients with PA than the patients with matched EH (65% vs 35%). In a large cardiovascular risk cohort, a higher circulating level of aldosterone was independently associated with echocardiographic parameters of concentric LVH.[41] These data imply that aldosterone has a direct prohypertrophic effect, independent of its effect of elevating blood pressure.

Regression of LVH after mineralocorticoid receptor blockade treatment in patients with PA has been demonstrated in many studies.[42–44] Gaddam *et al* reported that the degree of reversal of LVM that occurred after spironolactone treatment tended to be higher in the patients with PA with higher plasma aldosterone levels than in those with lower plasma aldosterone levels.[42] This dose-dependent effect may indicate the direct effect of aldosterone in the prevalence of LVH in patients with PA. Adrenalectomy is another treatment choice for patients with PA, and previous studies have shown obvious regression in LVM after adrenalectomy in patients with PA.[45 46] A previous meta-analysis[47] of prospective cohort studies compared the long-term effects of surgical adrenalectomy and treatment with mineralocorticoid receptor blockade, and the results revealed that surgical adrenalectomy had a 44% cure rate of hypertension and a lower requirement of additional antihypertensive medications than mineralocorticoid receptor blockade treatment. However, the reductions in LVM and cardiovascular outcomes were not different between surgical adrenalectomy and medical treatment, which may cause physicians to question the effects of surgical adrenalectomy in patients with PA. The superiority of surgical adrenalectomy over mineralocorticoid receptor blockade treatment remains unproven with regard to major adverse cardiovascular events. Further studies are warranted to investigate whether surgical adrenalectomy is better than mineralocorticoid receptor blockade for specific patients with PA. Such studies should also include a long enough follow-up period to assess cardiovascular risks.

Relative hyperfiltration is a specific phenomenon in patients with PA compared with patients with EH. Relative kidney hyperfiltration has been recognized as a cause of renal damage, and this may be due to the sodium-retaining effect of excess aldosterone.[48] Arima *et al*[49] reported that aldosterone may induce constriction of both afferent and efferent renal arterioles but with a higher effect on efferent arterioles, resulting in elevated glomerular capillary pressure and filtration fraction. Hyperfiltration also occurs in patients with diabetes mellitus. A meta-analysis of 10 cohort studies on patients with type 1 diabetes mellitus showed that patients with glomerular hyperfiltration subsequently had a higher risk of renal failure compared with patients without hyperfiltration.[50] Kuo *et al* also reported that relative kidney hyperfiltration is beyond the effect of hypertension in patients with PA.[51] Modest regression of kidney hyperfiltration after mineralocorticoid receptor blockade

Table 4 ANCOVA for LVMI among patients with primary aldosteronism and all patients

	Primary aldosteronism (n=168)		All patients (n=336)	
Source	F statistic	P value	F statistic	P value
eGFR, tertile	3.527	0.032	6.121	0.002
Age	0.632	0.428	0.020	0.887
Sex	7.536	0.007	10.848	0.001
Mean blood pressure	7.676	0.006	6.172	0.014
Hypertension duration	0.065	0.799	0.754	0.386
PA or EH	–	–	21.617	<0.001
Test for interaction*	–	–	0.802	0.449

* test the interaction between (tertile eGFR) and (PA or EH)

ANCOVA, analysis of covariance; eGFR, estimated glomerular filtration rate; EH, essential hypertension; LVMI, left ventricular mass index; PA, primary aldosteronism.

treatment in patients with PA has been reported.[52 53] A recent study also showed the modest effect of mineralocorticoid receptor blockade treatment in patients with PA compared with adrenalectomy and also a regression effect through different stages of chronic kidney disease.[54] This may imply that renal impairment is initiated by glomerular hyperfiltration which can be reversed after treatment.

In this study, we found that the relationship between eGFR and LVMI in the patients with PA was not linear, which was different to the negative linear relationship in the patients with EH. This implies that pressure overload is not the only effect to cause LVH in patients with PA. Relative kidney hyperfiltration with volume overload may play a role in LV remodeling in patients with PA. According to previous studies, a high level of circulating aldosterone may lead to target organ damage including increases in LVM and relative kidney hyperfiltration. Removing excess aldosterone with mineralocorticoid receptor blockade treatment or surgical adrenalectomy can reverse the effect of aldosterone to decrease LVM and eGFR as hyperfiltration influences the early post-treatment stage. This may suggest that excess aldosterone causes a reduction in eGFR secondary to renal damage. The processes of cardiac damage and renal damage were different according to our study. Our results expand the current evidence about the U-shaped relationship between LV structure and eGFR in patients with PA. A higher aldosterone level may initiate renal damage with relative kidney hyperfiltration and cardiac damage with LVH. This may explain why the patients with PA in the high tertile of eGFR had a higher LVMI compared with those in the medium tertile. As PA disease progresses, renal damage progresses resulting in a lower eGFR and the progression of cardiac damage to higher LVH. Our data showed that the patient with PA in the low tertile of eGFR had a higher LVMI compared with the medium tertile of eGFR. Although the difference in LVMI between the patients with PA in the low and high tertiles was not significant, there was a trend that the patients with PA in the low tertile had a higher LVMI compared with those in the high tertile. It is, therefore, important to diagnose PA and to initiate specific treatment in the early stage of PA because patients with PA have an increased cardiovascular risk compared with patients with EH. Our study demonstrated strong differences between cardiac and renal damage. The patients with PA with a high eGFR did not necessarily have a lower LVMI, but the patients with PA with a low eGFR had a higher LVMI. This provides a clinical indicator that can be used to predict the possible course of the disease early.

There are several limitations to this study. First, this is a cross-sectional study, so the causal relationship between LVMI and eGFR in the patients with PA could not be ascertained. The long-term tracking of LVMI and eGFR should be continued to demonstrate the sequential effect. The reversal of the effect on LVMI and eGFR after removing excess aldosterone may explain the possible sequential effect. Whether relative kidney hyperfiltration plays a role in LVH is still controversial. Second, major adverse cardiac events are more important than LVH. Our study did not have data on the cardiac outcomes. LVH is only a surrogate for future cardiovascular mortality and morbidity. However, previous studies have shown that LVH is a critical factor in cardiovascular outcomes.[12 55] Third, we did not adjust for antihypertension medication, which may affect LV structure and eGFR in patients with PA. Fourth, echocardiography may be to variable to measure LVM and cardiac magnetic resonance imaging (CMR) may be a more precise and reliable method. Our study did not use CMR to evaluate the LVH. However, both methods had strong correlations regardless of the echocardiography image quality.[56] Finally, the statistical significance of U-shape relationship between LVMI and eGFR in patients with PA was not very strong compared with linear relationship in patients with EH. Large sample size may be required to provide more accurate relationship between LVMI and eGFR in patients with PA.

CONCLUSION

The patients with PA in the medium tertile of eGFR were associated with a lower LVMI compared with those in the high and low tertiles of eGFR. This implies that there may be a U-shaped relationship between LVMI and eGFR in patients with PA, which is distinctly different to the negative linear relationship between LVMI and eGFR in patients with EH.

Contributors Conceptualization: Y-HL and C-SH. Methodology: M-TL and C-SH. Software: M-TL and C-SH. Validation: C-WL, C-HT, Y-YC, Z-WC, S-FK, and L-CL. Formal analysis: M-TL and C-SH. Investigation: M-TL and X-MW. Resources: Y-HL. Data curation: M-TL and Y-HL. Writing—original draft preparation: M-TL. Writing—review and editing: C-SH and Y-HL. Visualization: M-TL and C-TP. Supervision: V-CW and Y-HL. Project administration: Y-HL. Funding acquisition, Y-HL.

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Data availability statement Data are available on reasonable request.

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