Impact of Adrenalectomy on Diastolic Cardiac Dysfunction in Patients with Primary Aldosteronism

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Poor prognostic cardiac function is known among some patients with primary aldosteronism (PA). However, studies with echocardiograms on whether the normalization of aldosterone after laparoscopic adrenalectomy (LADX) improves myocardial hypertrophy and diastolic cardiac dysfunction have been inadequate. Between August 2009 and December 2021, 147 patients with unilateral PA who underwent pre- and post-LADX echocardiography at a single center were enrolled in this retrospective study. We evaluated the cardiac impact of LADX by comparing patients who demonstrated complete clinical success (CS) with those who demonstrated partial or absent CS. Adjusted odds ratios (ORs) for not obtaining complete CS were calculated using binomial logistic regression analysis for clinically significant items among the pre- and postoperative clinical and echocardiographic markers. Overall, 47 (29%) and 104 (71%) patients had complete and partial or absent CS, respectively. Compared to patients with complete CS, patients with partial CS or without CS tended to have preoperative low early to late diastolic transmitral flow velocity (E/A) (< 0.8 cm/s) (41% vs. 21%, $P < 0.05$) and postoperative supranormal left ventricular ejection fraction (LVEF) (> 70%) (37% vs. 21%, $P < 0.05$). Furthermore, laparoscopic adrenalectomy improved the low and high echocardiographic values of E/A and LVEF, respectively, in both groups. The risk factors for not reaching complete CS were male sex (OR 3.42), low preoperative E/A (OR 3.11), and postoperative supranormal LVEF (OR 3.17). Although low preoperative E/A and postoperative supranormal LVEF are associated with poor clinical outcomes, LADX can improve diastolic cardiac function in patients with PA.

Keywords: early to late diastolic transmitral flow velocity; echocardiography; laparoscopic adrenalectomy; primary aldosteronism; supranormal ejection fraction
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Introduction

Primary aldosteronism (PA) is characterized by excessive renin-independent endogenous aldosterone production from adrenal adenomas or hyperplasia. In addition to inducing high blood pressure, high aldosterone levels have been recently recognized to affect various organs through mineralocorticoid receptors (MR). Cardiomyocytes highly express MR, and aldosterone acts directly on the myocardium via MR and the blood pressure-increasing effect of volume loading. The direct action of aldosterone causes left ventricular (LV) remodeling and dysfunction through three mechanisms: muscle cell hypertrophy, chronic inflammation, and extracellular matrix metabolism dysregulation (Tsai et al. 2021). LV remodeling can also lead to systolic and diastolic cardiac dysfunction of the left ventricle and unfavorable outcomes, including heart failure, atrial fibrillation, and malignant arrhythmias (González et al. 2018).

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LV remodeling in PA results in LV hypertrophy and fibrosis, and resembles hypertrophic cardiomyopathy (Tsai et al. 2021). However, the initial stage of hypertrophic cardiomyopathy is asymptomatic, and echocardiography shows diastolic cardiac dysfunction and supranormal LV ejection fraction (LVEF). As remodeling progresses, LVEF becomes normal. Subsequently, cardiac function cannot be completely compensated for some patients, resulting in diminished contractile dysfunction with decreased LVEF (Olivotto et al. 2012). Recent large-scale observational studies have shown that supranormal LVEF (≥ 70%) is associated with high mortality rates (Ng and Bax 2019). Excessive aldosterone upregulates the sympathetic nervous system, leading to increased cardiac output, high arterial stiffness, and high intravascular volume load (Kontak et al. 2010; Choudhary et al. 2021). However, the significance of supranormal LVEF in PA has not yet been elucidated.

The LVEF, early to late diastolic transmitral flow velocity (E/A), early mitral inflow velocity to early diastolic mitral annular tissue velocity (E/e'), and LV mass index (LVMI) are important echocardiographic findings in patients with PA. The LVEF is mainly used to evaluate the contractile functions of the heart. LVMI is a body surface area-corrected version of LV weight that reflects LV hypertrophy reported to predict patients with heart failure who maintain LVEF with LV enlargement (Yamanaka et al. 2020). The E/A and E/e' are essential for diagnosing diastolic cardiac dysfunction (Mitter et al. 2017). Previous reports have shown that patients with hyperaldosteronism have reduced E/A and increased E/e' compared with healthy individuals (Cesari et al. 2016). The prevalence of diastolic cardiac dysfunction is 35% in patients with PA, which is three times higher than that in healthy individuals (12%) (Cesari et al. 2016).

Laparoscopic adrenalectomy (LADX) is recommended for treating unilateral adrenocortical PAs after a localized diagnosis of unilateral PA has been confirmed by adrenal vein sampling (Funder et al. 2016). Laparoscopic adrenalectomy in patients with PA reduces mortality by 73% and the likelihood of developing chronic heart failure by 45% (Huang et al. 2019). Moreover, LADX improves the quality of life in patients with PA (Ishidoya et al. 2019; Kawasaki et al. 2023). Since cases with LV remodeling are associated with poor prognosis, long-term follow-up is required after LADX for cases of PA with LV remodeling. Studies on the early effects of LADX on patients with PA and diastolic cardiac dysfunction are still inadequate. Therefore, this study aimed to clarify the effects of LADX on patients with PA and determine whether the normalization of aldosterone levels after LADX improves myocardial hypertrophy and diastolic cardiac dysfunction.

Materials and Methods

Patients

Patients with unilateral PA who underwent LADX between August 2009 and April 2021 in the Tohoku University Hospital were eligible for inclusion in this study. Adrenal venous sampling was performed to determine whether the adrenal lesion was unilateral or bilateral (Satoh et al. 2007).

Study design

Details on age at the time of LADX, observation period, duration of hypertension, sex, complications, body mass index, maximum tumor size, surgical duration, and the period between LADX and post-LADX echocardiography were noted. The duration of hypertension was defined as the years between the self-reported hypertension onset and the time of LADX. Data on pre- and post-LADX clinical variables, including systolic blood pressure (sBP), diastolic blood pressure (dBP), echocardiographic findings, the use of oral antihypertensive agents, serum creatinine concentration, serum potassium concentration, plasma renin activity (PRA), and plasma aldosterone concentration (PAC), were collected. PAC was measured using radioimmunoassay. Most patients were discharged after blood collection 1 week after the operation. Additionally, the aldosterone/renin ratio was calculated.

LADX procedure

The LADX procedure was performed according to Smith's Textbook of Endourology (Matsuda et al. 2019). Briefly, LADX is performed via 3-4 holes in the trunk, through which a camera or forceps is inserted. The tumor is subsequently peeled off and removed while viewing the screen. The tumor expands the camera port by 2-3 cm and is pulled out of the body through this aperture.

Study protocol

We investigated the relationship between echocardiographic findings before and after LADX (i.e., LVEF, LVMI, E/A, and lateral E/e'), and whether patients with PA reached complete clinical success (CS). According to an international consensus, complete CS was defined as the achievement of normal blood pressure (sBP < 140 mmHg and dBP < 90 mmHg) without the use of antihypertensive drugs postoperatively, and partial or absent CS was defined as having high blood pressure or the use of antihypertensive drugs postoperatively (Williams et al. 2017). For comparison, patients were categorized into groups based on low, normal, and high values of echocardiographic parameters. Pre-LADX LVEF was classified as follows: < 60%, 60%-70%, and ≥ 70%. Due to the limited sample size and high mortality rate associated with LVEF ≥ 70%, the supranormal LVEF was defined as ≥ 70% (Wehner et al. 2020). The pre-LADX LVMI was as follows: high LVMI (males, > 120 g/m^2 and females, > 100 g/m^2) and normal LVMI (males, ≤ 120 g/m^2 and females, ≤ 100 g/m^2). Pre-LADX E/A was classified as < 0.8 cm/s or ≥ 0.8 cm/s (Mitter et al. 2017). Pre-LADX lateral E/e' was categorized as < 8 or ≥ 8 mmHg (Mitter et al. 2017; Williams et al. 2017).

Statistical analysis

Student's unpaired t-test and chi-square test were used to compare the two groups. Adjusted odds ratios (ORs) were calculated using binomial logistic regression analysis for clinically significant items among the pre- and postoperative clinical and echocardiographic markers. A P-value of < 0.05 was considered statistically significant. Data were analyzed using JMP® Pro software (SAS Institute Inc., Cary, NC, USA).

Ethics committee approval

The protocol for this research project was approved by the institutional ethics committee of the Tohoku University Hospital (approval number: 2021-1-403). The study conformed to the provisions of the Declaration of Helsinki, and written informed consent was obtained from all participants.

Results

Overall, 258 patients with unilateral PA who underwent LADX were eligible for inclusion. Of these, 167 patients underwent follow-up echocardiography. In total, 20 patients were excluded, including 19 patients with no preoperative E/A measurement data and one patient with an E/A > 2. Furthermore, 147 patients with unilateral PA who underwent LADX were included in the analysis.

The median patient age was 55 years [interquartile range (IQR), 44-63], and 61% of the patients were male (Table 1). Of the 147 patients, 18%, 46%, 10%, and 12% had type 2 diabetes, chronic renal failure, a history of stroke, and a history of heart disease, respectively. The median period between surgery and echocardiography was 12 months (IQR, 11-13). Complete CS was observed in 43 (29%) of 147 patients, and 104 demonstrated partial or absent CS. The complete CS group had more females (58% vs. 32%, P = 0.003), significantly lower preoperative levels of antihypertensive agent use (4 vs. 5 tablets, P = 0.021), and a shorter duration of hypertension (6 vs. 11 years, P = 0.032) than the partial or absent CS group. Surgical items (length of stay, operative time, and tumor size) and postoperative blood sampling data are listed in Supplementary Table S1.

Changes in LVEF before and after surgery between patients with LVEF < 60% as the low value (N = 18) and those with LVEF ≥ 70% as the high value (N = 54) were compared. Additionally, the group with LVEF 60%-70% was also analyzed (N = 75). Compared to the 60%-70%-LVEF group, a significant increase of 5.6% (P < 0.05) was observed in the < 60%-LVEF group, and a significant decrease of 3.8% (P < 0.05) was observed in the ≥ 70%-LVEF group.

Regardless of low or high preoperative LVEF, the postoperative echocardiographic findings were close to the normal range (Fig. 1). Additionally, echocardiographic findings significantly improved postoperatively in low and high preoperative LVMI cases (females ≤ 100 g/m^2 and males ≤ 120 g/m^2, and females > 100 g/m^2 and males > 120 g/m^2, respectively). In patients with high preoperative

Table 1. Clinical variables of patients with primary aldosteronism stratified based on the achievement of clinical success.

Variables*	Total 147	Complete CS 43	Partial or Absent CS 104	Complete CS vs. Partial or Absent CS P-value*
Age, years, median (IQR)	55 (44-63)	55 (43-62)	55 (47-63)	0.116
BMI, kg/m^2, median (IQR)	24.8 (22.1-26.5)	24.2 (21.7-25.9)	25.0 (22.3-27.0)	0.287
Hypertension duration, month, median (IQR)	10 (3-19)	6 (2-18)	11 (5-20)	0.032*
Period between LADX and echocardiograms, month, median (IQR)	12 (11-13)	12 (11-13)	12 (11-14)	0.840
Pre-LADX PAC, ng/dl, mean (SD)	86.1 (113.2)	75.8 (84.5)	90.4 (123.3)	0.903
Pre-LADX PRA, ng/ml/hr, mean (SD)	0.9 (1.8)	0.7 (1.3)	1.0 (2.0)	0.382
Pre-LADX ARR, PAC/PRA, mean (SD)	394.3 (832.3)	300.6 (402.9)	433.0 (954.3)	0.592
Pre-LADX serum potassium, mEq/L, mean (SD)	3.9 (0.8)	3.8 (0.7)	3.9 (0.8)	0.231
Pre-LADX sBP, mmHg, mean (SD)	140.2 (17.5)	137.0 (17.7)	141.5 (17.3)	0.163
Pre-LADX dBP, mmHg, mean (SD)	91.3 (12.1)	90.0 (11.3)	91.9 (12.5)	0.409
Pre-LADX antihypertensive agents, tablet, median (IQR)	5 (2-8)	4 (2-6)	5 (3-8)	0.021*
Males, number (%)	89 (61)	18 (42)	71 (68)	0.003*
SAS, number (%)	68 (46)	15 (35)	53 (51)	0.075
DM, number (%)	26 (18)	6 (14)	20 (19)	0.446
CKD, number (%)	68 (46)	15 (35)	53 (51)	0.075
Cerebral stroke, number (%)	14 (10)	5 (12)	9 (9)	0.576
Cardiac disorder, number (%)	12 (8)	3 (7)	9 (9)	0.736

*P-value was determined by the t-test for the clinical continuous variable, and the chi-square test for the clinical categorical variable.
CS, clinical success; IQR, interquartile range; SD, standard deviation; BMI, body mass index; ARR, aldosterone-renin ratio; PAC, plasma aldosterone concentration; PRA, plasma renin activity; LADX, laparoscopic adrenalectomy; sBP, systolic blood pressure; dBP, diastolic blood pressure; SAS, sleep apnea syndrome; DM, diabetes mellitus; CKD, chronic kidney disease.

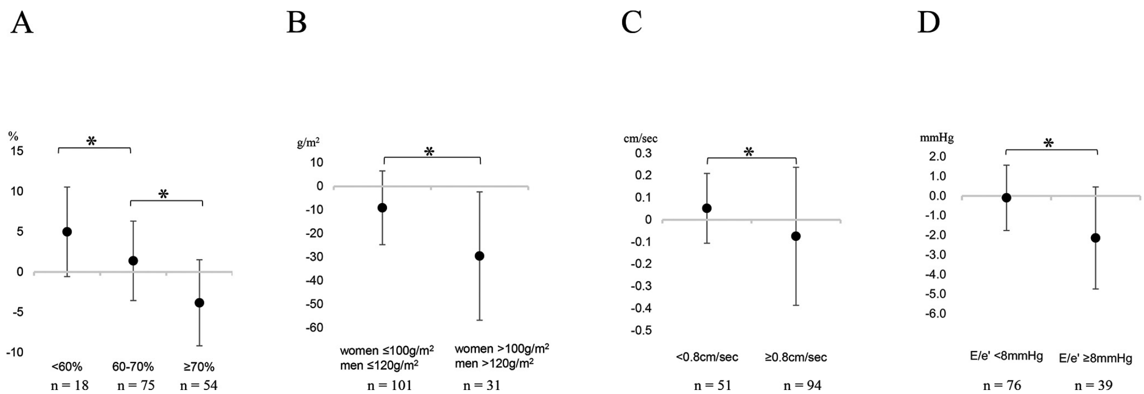

Fig. 1. Cardiac function and extent of change before and after LADX.
The differences were evaluated using t-test, and a P-value < 0.05 was considered significant. Each error bar indicates the standard deviation. (A) LVEF change between pre- and post-surgery stratified for the pre-surgery LVEF group. The mean variations in LVEF were significant among the pre-LADX groups (Δ5.0, Δ1.4, and Δ−3.8% for < 60%, 60%-70%, and ≥ 70%, respectively; *P < 0.05). (B) Left ventricular mass index (LVMI) change between pre- and post-surgery stratified for the pre-surgery LVMI group. The mean differences in LVMI were significant based on the pre-LADX LVMI groups (Δ−9.1 for females ≤ 100 g/m^2 and males ≤ 120 g/m^2 and Δ−29.6 g/m^2 for females > 100 g/m^2 and males > 120 g/m^2; *P < 0.05) (C) The early to late diastolic transmitral flow velocity (E/A) change between pre- and post-surgery stratified for the pre-surgery E/A group. The mean change in E/A was significant (Δ−0.07 vs. Δ0.05 for ≥ 0.8 vs. < 0.8 cm/s, respectively; *P < 0.05). (D) Early mitral inflow velocity to early diastolic mitral annular tissue velocity (E/e') change between pre- and post-surgery stratified for the pre-surgery E/e' group. The mean variations in lateral E/e' were significant among the pre-LADX groups (Δ−0.1 vs. Δ−2.1 for < 8 vs. ≥ 8 cm/s, respectively; *P < 0.05). LADX, laparoscopic adrenalectomy; LVEF, left ventricular ejection fraction.

LVMI (N = 31), LVMI significantly decreased postoperatively regarding the preoperative value (−29.6 g/m^2, P < 0.05). Even in cases with low preoperative E/A (< 0.8 cm/s) (N = 51), a significant improvement was observed postoperatively (Δ + 0.05 cm/s, P < 0.05). Regarding the lateral E/e', a significant improvement was observed in cases with high preoperative LVMI (≥ 8 mmHg and Δ−2.1 mmHg) (N = 39) compared with that in those with low preoperative LVMI (< 8 mmHg) (N = 76). All evaluated echocardiographic findings improved postoperatively, and LADX improved cardiac function in patients with PA.

Compared with the partial or absent CS group, the proportion of cases with significantly low preoperative E/A was higher in the complete CS group (41% vs. 21%, P = 0.019) (Table 2). Although no significant difference was found in the preoperative supranormal LVEF rate between the groups, in the complete CS group, the proportion of patients with supranormal LVEF postoperatively was higher than in the partial or absent CS group (37% vs. 21%, P = 0.049).

Fig. 2 shows the regression line for the change in cardiac function pre- and postoperatively according to echocardiographic parameters, including LVEF, LVMI, E/A, and lateral E/e'. All four parameters showed a linear relationship to reach the normal range postoperatively. The gradient of the regression line for E/A was significantly greater in the partial or absent CS group than that in the complete CS group (0.00 vs. −0.33, P < 0.05, analysis of covariance) (Fig. 2C). However, no difference was found in the gradient of the regression lines for LVEF, LVMI, and lateral E/e' between the groups (Fig. 2A, B and D).

Complete CS was achieved in 29% of the cases postoperatively in this study. As described above, in the univariate analysis, sex, duration of hypertension, surgical duration, number of antihypertensive agents, low preoperative E/A, and postoperative supranormal LVEF were associated with not achieving complete CS postoperatively (Tables 1 and 3). The adjusted binomial logistic analysis for these seven factors demonstrated that the risk factors for not achieving complete CS postoperatively were male sex, low preoperative E/A, and postoperative supranormal LVEF (Table 3). The ORs for not achieving complete CS, according to the male sex, low preoperative E/A, and postoperative supranormal LVEF were 3.42 [95% confidence interval (CI) = 1.44-8.11, P < 0.05], 3.11 (95% CI = 1.10-8.78, P < 0.05), and 3.17 (95% CI = 1.23-8.24, P < 0.05), respectively.

Discussion

The highlight of this study is the echocardiographic evaluation of the cardiac function associated with complete CS and partial or absent CS after LADX in patients with PA. The novelty of this study is that it investigated the relationship between supranormal LVEF and low E/A and CS after LADX. Supranormal LVEF generally implies an LVEF > 65% and an adverse prognosis. Wehner et al. (2020) reported in a large population study that an LVEF ≥ 70% had an adjusted hazard ratio (HR) for death more comparable to that with an LVEF between 35% and 40% than that with an LVEF between 60% and 65% (1.71, 95% CI; 1.64-1.77 vs. 1.73, 95% CI; 1.66-1.80). A theory is that the supranormal LVEF in hypertrophic cardiomyopathy can be

Table 2. Patients with primary aldosteronism classified based on the markers of cardiac function in the clinical success groups.

	Total 147		Complete CS 43		Partial or Absent CS 104		Complete CS vs. Partial or Absent CS	
Clinical categorical variable*	pre-LADX	post-LADX	pre-LADX	post-LADX	pre-LADX	post-LADX	pre-LADX	post-LADX
LVEF, number (%)								
LVEF < 60%	18 (12)	17 (12)	3 (7)	3 (7)	15 (14)	14 (13)	0.437	0.049*
60% ≤ LVEF < 70%	75 (51)	83 (56)	24 (56)	31 (72)	51 (49)	52 (50)		
LVEF ≥ 70%	54 (37)	47 (32)	16 (37)	9 (21)	38 (37)	38 (37)		
E/A, number (%)								
< 0.8 cm/s	52 (35)	54 (37)	9 (21)	11 (26)	43 (41)	43 (42)	0.019*	0.059
≥ 0.8 cm/s	95 (65)	91 (63)	34 (79)	32 (74)	61 (59)	59 (58)		
LVMI, number (%)								
male < 120 g/m^2, female < 100 g/m^2	102 (77)	111 (78)	35 (85)	37 (88)	67 (73)	74 (73)	0.114	0.053
male ≥ 120 g/m^2, female ≥ 100 g/m^2	31 (23)	32 (22)	6 (15)	5 (12)	25 (27)	27 (27)		
lateral E/e', number (%)								
< 8 mmHg	78 (65)	98 (72)	27 (73)	32 (78)	51 (61)	66 (69)	0.222	0.306
≥ 8 mmHg	42 (35)	38 (28)	10 (27)	9 (22)	32 (39)	29 (31)		

*P-value was determined using the the chi-square test for the categorical variables separately pre- and post-LADX.
CS, clinical success; LADX, laparoscopic adrenalectomy; LVEF, left ventricular ejection fraction; E/A, early to late diastolic transmitral flow velocity; LVMI, left ventricular mass index; E/e', E to early diastolic mitral annular tissue velocity.

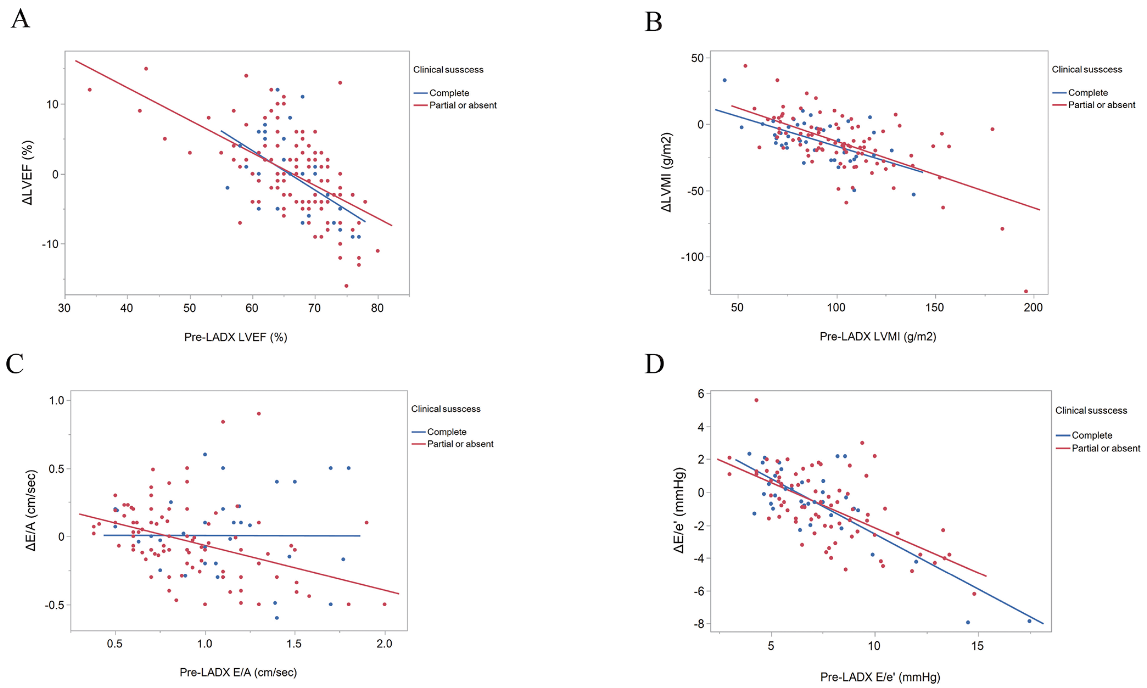

Fig. 2. Regression lines for cardiac function and extent of change before and after LADX as classified by clinical success (CS).
The slope differences were evaluated using analysis of covariance, and a P-value < 0.05 was considered significant. (A) The slope of the regression line for left ventricular ejection fraction (LVEF) and changes in LVEF were significantly high among CS groups (ΔLVEF = 37.1 − 0.6 × LVEF and ΔLVEF = 30.9 − 0.5 × LVEF for complete and partial or absent CS, respectively; P = 0.52). (B) Slope of the regression line in the left ventricular mass index (LVMI) and changes in LVMI were not different among CS groups (ΔLVMI = 28.1 − 0.5 × LVMI and ΔLVMI = 37.1 − 0.5 × LVMI for complete and partial or absent CS, respectively; P = 0.71). (C) The slope of the regression line in early to late diastolic transmitral flow velocity (E/A) and changes in E/A were significantly high among CS groups (ΔE/A = 0.00 − 0.00 × E/A and ΔE/A = 0.26 − 0.33 × E/A for complete and partial or absent CS, respectively; P < 0.05). (D) The slope of the regression line in lateral E to early diastolic mitral annular tissue velocity (E/e') and changes in lateral E/e' were not different among CS groups (ΔE/e' = 4.2 − 0.7 × E/e' and ΔE/e' = 3.3 − 0.6 × E/e' for complete and partial or absent CS, respectively; P = 0.31). LADX, laparoscopic adrenalectomy.

Table 3. Multivariate logistic regression analysis of clinical and echocardiographic parameters associated with partial or absent clinical success of patients with primary aldosteronism.

	Multivariate analysis		
	Odds ratio	95% CI	P-value
Age at LADX			
< 55 year		reference	
≥ 55 year	2.00	0.70-5.70	0.194
Sex			
Females		reference	
Males	3.42	1.44-8.11	0.005*
Duration of hypertension			
< 10 years		reference	
≥ 10 years	1.38	0.55-3.50	0.492
Antihypertensive agents			
< 5 agents		reference	
≥ 5 agents	1.48	0.66-3.30	0.337
Pre-LADX E/A			
< 0.8 cm/sec	3.11	1.10-8.78	0.032*
≥ 0.8 cm/sec		reference	
Post-LADX LVEF			
LVEF < 60%	1.74	0.43-7.04	0.462
60% ≤ LVEF < 70%		reference	
LVEF ≥ 70%	3.17	1.23-8.24	0.028*

*P < 0.05.
LADX, laparoscopic adrenalectomy; E/A, early to late diastolic transmitral flow velocity; LVEF, left ventricular ejection fraction.

attributed to reduced LV end-diastolic volume due to LV hypertrophy and decreased LV end-systolic volume for maintenance of the cardiac output, which thereby increases the LVEF. This phenomenon was also shown in the murine model of hypertrophic obstructive cardiomyopathy (Sørensen et al. 2016), suggesting that an LVEF ≥ 70% is a novel high-risk factor that is associated with hypertrophic cardiomyopathy.

Both supranormal LVEF and low E/A are associated with high mortality rates and have recently been found to be early pathological features of cardiac hypertrophy (Bella et al. 2002; Hudson and Pettit 2020). Although hypertensive patients with diastolic cardiac dysfunction are frequently asymptomatic, diastolic cardiac dysfunction is closely associated with the development of heart failure with preserved ejection fraction (HFpEF) (Aurigemma et al. 2001; Redfield et al. 2003; Solomon et al. 2010). In this study, achieving complete CS with LADX was difficult in cases of postoperative supranormal LVEF and low preoperative E/A. Excess aldosterone and antihypertensive agents might influence cardiac functions (Kontak et al. 2010; Lam et al. 2013). Therefore, postoperative cardiac function evaluation may help more accurately determine the remodeling and risk of heart failure related to life-threatening complications. We found that LADX suppressed supranormal LVEF and improved diastolic function, and thus, may also lead to the suppression of the onset of heart failure.

In this study, LADX helped achieve complete CS in 29% of the patients with PA; female sex, the duration of hypertension, surgical duration, and the number of antihypertensive medications were significantly associated with complete CS. According to a previous large cohort study, complete CS was achieved in 32.6% of the patients with PA and was reportedly associated with age, female sex, duration of hypertension, body mass index, and the number of antihypertensive drugs, similar to the results of this study (Morisaki et al. 2019). In a multivariate analysis adjusted for risk factors for not achieving complete CS, we demonstrated for the first time that echocardiographic findings, such as low preoperative E/A and postoperative supranormal LVEF, could influence the clinical efficacy of LADX in patients with PA.

The improvement in cardiac function after LADX was confirmed in patients with low and high values preoperatively. Chang et al. (2019) reported that patients with PA had worse LV diastolic function than patients with essential hypertension, which could be managed by surgery. Similarly, in this study, improvement in postoperative echocardiographic findings was observed in both the complete CS and partial or absent CS groups. However, E/A showed better postoperative improvement in patients with partial or absent CS. Pseudonormalization of the E/A pattern may influence this phenomenon. Therefore, cases with an E/A > 2 and a suspected pseudonormalization pattern were excluded from our analysis. Additionally, since E/A cannot be measured in patients with atrial fibrillation, this analysis did not include cases of atrial fibrillation.

As shown in Fig. 1A, a significant improvement in LVEF after LADX was observed in cases with an LVEF < 60%. Further, as shown in Fig. 2, a remarkable improvement in LVEF was observed in 16 of 18 cases (89%) with low LVEF. We believe that PA, including hypertrophic cardiomyopathy, progresses from mild diastolic dysfunction to HFpEF (LVEF ≥ 50%) and finally to heart failure with midrange LVEF (heart failure with midrange ejection fraction, HFmEF; LVEF 40-49%) and heart failure with reduced LVEF (heart failure with reduced ejection fraction, HFrEF; LVEF < 40%). Four patients were included in HFmEF and HFrEF before LADX, whereas only one was included in HFmEF LVEF after LADX (Supplementary Table S2). Therefore, we suggest that LADX can be expected to improve LVEF in patients with PA with moderate chronic heart failure. Thus far, some studies have reported improvement in LVEF after LADX based on several case reports (Alvarez and Mohan 2018; Sato et al. 2019); however, the extent to which LADX is effective in abnormal LVEF cases remains unclear, and further case studies are needed to reach a conclusion in this regard.

This study had some limitations. First, due to its single-center, retrospective observational design, the possibility of selection bias cannot be excluded. Second, the sample size was insufficient for a more precise echocardiographic analysis of cardiac function. Echocardiography is limited in accuracy and reproducibility; therefore, an alternative method, such as cardiac magnetic resonance imaging, should have also been employed (Frustaci et al. 2019). Furthermore, more detailed echocardiographic data were needed to accurately analyze diastolic cardiac function. However, this study is the largest report evaluating echocardiographic findings before and after LADX in patients with PA, and it is the first to analyze the relationship between CS and the effects of LADX on diastolic cardiac function and supranormal LVEF. Therefore, in the future, we would like to evaluate a larger number of participants in a prospective study.

In conclusion, excess aldosterone resulted in low preoperative E/A and postoperative supranormal LVEF, which were associated with partial or absent CS after LADX. However, regardless of the degree of CS, the usefulness of LADX was demonstrated in terms of improved cardiac function based on echocardiographic assessment in patients with PA.

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Conflict of Interest

The authors declare no conflict of interest.

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Supplementary Files

Please find supplementary file(s);
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