

## Long-Term Results of Laparoscopic Partial Versus Total Adrenalectomy for Aldosterone Producing Adenoma

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**Purpose:** Laparoscopy surgery is the gold standard for the treatment of aldosterone-producing adenomas (APA). However, the effectiveness between laparoscopic total and partial adrenalectomy is controversial. Therefore, we retrospectively analyzed the postoperative and follow-up outcomes of these two procedures.

**Materials and Methods:** A total of 96 APA patients underwent laparoscopic surgery in our hospital between January 2012 and December 2017. A total of 65 patients who underwent laparoscopic partial adrenalectomy (group 1) were compared with 31 patients who underwent laparoscopic total adrenalectomy (group 2). The mean follow-up time was 32.3 months and 40.8 months, respectively. Patient's preoperative characteristics, date during surgery, and postoperative clinical results of the two groups were analyzed.

**Results:** In both groups of patients, laparoscopic adrenalectomy was successfully carried out. The laparoscopic partial adrenalectomy group had a shorter operation time when compared to total adrenalectomy ( $P = .01$ ). However, patients in the laparoscopic total adrenalectomy group were older ( $P = .04$ ) and had a higher proportion of multiple adenomas ( $P = .01$ ) compared to partial adrenalectomy. Five patients (7.7%) who underwent partial adrenalectomy did not show improvement in hypertension and/or serum potassium below normal levels, and review of plasma aldosterone concentration (PAC) and/or computerized tomography (CT) indicated that surgery was not successful in these patients. All 31 patients who underwent total adrenalectomy showed improvement or recovery from hypertension, and all PAC and serum potassium levels returned to normal levels after surgery.

**Conclusion:** Although both surgical procedures were technically safe and feasible, laparoscopic partial adrenalectomy showed a higher failure rate (7.7%) for patients with APA. Therefore, choosing laparoscopic partial adrenalectomy requires careful consideration, and we selected laparoscopic total adrenalectomy in patients with unilateral APA.

**Keywords:** adrenalectomy; aldosterone producing adenoma; hyperaldosteronism; laparoscopy; partial

### INTRODUCTION

Primary aldosteronism (PA), described for the first time in 1955 by Conn et al., is characterized by excessive aldosterone secretion, and leads to secondary hypertension, hypokalemia, hypervolemia, and metabolic alkalosis.<sup>(1)</sup> PA accounts for ~10% of patients with hypertension, which is the most common cause of secondary hypertension.<sup>(2)</sup> Clinical subtypes of PA include aldosterone producing adenoma (APA), unilateral adrenal hyperplasia (UAH), and idiopathic aldosteronism (IAH).<sup>(3)</sup> Laparoscopic adrenalectomy is the preferred treatment for APA or UAH. In case of IAH, medical treatment for mineralocorticoid receptor antagonist (MRA) is recommended.<sup>(2)</sup> The advantage of partial adrenalectomy is that it retains

a portion of the adrenal gland on the affected side. This surgical procedure is minimal for adrenal function impairment. If the other adrenal gland develops a lesion, it can provide an opportunity for reoperation. The 2014 Chinese Urological Association(CUA) guidelines recommend laparoscopic adrenalectomy for APA, thereby retaining adrenal tissue as much as possible. In recent years, several studies have shown that laparoscopic total adrenalectomy has clear beneficial effects on the treatment of APA. Unilateral adrenalectomy abolished aldosterone hypersecretion and hypokalemia in most patients with unilateral aldosterone hypersecretion.<sup>(4)</sup> Hennings et al. confirmed that after long-term follow-up, unilateral total adrenalectomy had a significant effect on the treatment of APA.<sup>(5)</sup> However, few reports

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**Table 1.** Clinical characteristics of 96 patients with APA.

	Laparoscopic partial adrenalectomy (n = 65)	Laparoscopic total adrenalectomy (n = 31)	P
Age (years)	48.27 ± 11.47	56.42 ± 16.42	.04
Male / female	22 / 43	12 / 19	.64
Tumor site (Left / Right)	38 / 27	18 / 13	.97
Tumor diameter (cm)	1.86 ± 0.65	1.96 ± 0.96	.67
Blood pressure (mmHg)			
Systolic BP	166.52 ± 24.04	174.00 ± 36.06	.37
Diastolic BP	101.00 ± 14.12	100.75 ± 21.44	.96
Serum potassium (mmol/L)	2.55 ± 0.72	2.37 ± 0.63	.42
PAC (ng/dL)	26.65 ± 6.89	27.29 ± 7.60	.75
ARR (ng/dL/ng/mL/h)	249.16 ± 192.42	237.58 ± 259.05	.87
Follow-up time (months)	32.32 ± 19.04	40.81 ± 28.09	.18

Data are expressed as the mean ± SD.

**Abbreviations:** BP, blood pressure; Serum K<sup>+</sup> normal value 3.5–5.5 mmol/L; APA, aldosterone-producing adenoma; PAC; plasma aldosterone concentration; PAC normal value 0.7–15 ng/dL; ARR: plasma aldosterone concentration to renin activity ratio.

supported partial adrenalectomy of APA. Our objective was to assess the safety, feasibility, and efficacy of laparoscopic partial versus total adrenalectomy in patients with APA.

## PATIENTS AND METHODS

### Study Population

A total of 96 patients who underwent laparoscopic partial adrenalectomy or laparoscopic total adrenalectomy for APA were retrospectively analyzed between January 2012 and December 2017. This retrospective study was approved by the ethics committee of the First Affiliated Hospital of Soochow University (Clinical trial identifier: 2011045). The APA procedure included the following diagnostic steps: (1) All patients had hypokalemia, persistent hypertension, and biochemical evidence of hyperaldosteronism. Biochemical evidence of hyperaldosteronism was defined as a plasma aldosterone concentration (PAC) ≥ 20 ng/dL, and a plasma aldosterone-plasma renin activity ratio (ARR) ≥ 40 ng/dL/ng/mL/h. (2) All patients underwent computerized tomography (CT) preoperatively. CT confirmed that all patients had unilateral adrenal adenomas, and in patients with UAH, adenomas in the bilateral adrenals or IHA were excluded from the study.

### Procedures

All patients underwent retroperitoneal laparoscopic adrenalectomy. A total of 65 out of 96 APA patients underwent laparoscopic partial adrenalectomy. The criteria for partial adrenalectomy included a single adenoma at the surface or in the lateral branch of the adrenal gland associated with lots of normal adrenal tissue. Laparoscopic partial adrenalectomy was executed by approaching the tumor directly without controlling

the adrenal vessels. Laparoscopic partial adrenalectomy required complete resection of the tumor and normal adrenal tissue 5mm away from the tumor. In general, hem-o-lok clips were used to control bleeding from the adrenal incision. If a single adenoma tumor was present in the middle of the adrenal gland, laparoscopic total adrenalectomy was performed. In our study, 4 individual surgeons performed laparoscopic adrenalectomy, whereas one surgeon performed total adrenalectomy for all APA patients. Laparoscopic unilateral total adrenalectomy was performed in 31 out of 96 APA patients, and involved complete removal of the adrenal gland by double ligation of the central adrenal vein using hem-o-lok clips.

### Evaluations

In this study, differences in patient characteristics of preoperative, operative time, and intraoperative blood loss were compared between the two groups. Postoperative follow-up included blood pressure recording, serum potassium levels, PAC and imaging date. Normal blood pressure without treatment was defined as hypertension cure, and the achievement of a normal blood pressure using fewer drugs than before adrenalectomy was defined as an improvement. In the laparoscopic partial adrenalectomy group, the mean postoperative follow-up time was 32.3 months, whereas in the laparoscopic total adrenalectomy group, the follow-up time was 40.8 months.

### Statistical Analysis

Statistical analyses were performed using SPSS® version 20.0 software. Numeric data of a normal distribution was expressed as the mean ± standard deviation (x ± SD) and were analyzed using the Student's t test. Pearson's chi-square test was used to compare categor-

**Table 2.** Postoperative and follow-up outcomes when comparing laparoscopic total versus partial adrenalectomy.

	Laparoscopic partial adrenalectomy (n = 65)	Laparoscopic total adrenalectomy (n = 31)	P
Operative time (minutes)	76.16 ± 25.82	105.33 ± 29.60	.01
Blood loss (mL)	60.54 ± 51.91	69.55 ± 66.20	.62
Multiple adenomas (n)	0 (0%)	6 (19.4%)	.01
Cured hypertension (n)	37 (56.9%)	17 (54.8%)	.85
Improved hypertension (n)	23 (35.4%)	14 (45.2%)	.36
No improved hypertension (n)	5 (7.7%)	0 (0%)	.17
Hypokalaemia (n)	3 (4.6%)	0 (0%)	.55
No improvement of PA (n)	5 (7.7%)	0 (0%)	.27

Data are expressed as the mean ± SD or percentage in parentheses. Serum K<sup>+</sup> normal value 3.5–5.5 mmol/L; PA, primary aldosteronism.

**Table 3.** No improvement of primary aldosteronism in 5 aldosterone-producing adenoma patients who underwent laparoscopic partial adrenalectomy.

	Blood pressure	Serum potassium levels	PAC and others
Case 1	Remained hypertensive	3.0 mmol/L at one month after surgery; 2.21 mmol/L at 12 months after surgery; continuous oral potassium supplementation.	CT confirmed tumor recurrence (FIG. 1). The PAC was 25.7 ng/dL after 36 months of follow-up.
Case 2	Remained hypertensive	2.9 mmol/L at one month after surgery; continuous oral potassium supplementation.	CT confirmed tumor recurrence (FIG. 2). The PAC was 15.21 ng/dL after 22 months of follow-up. The PAC after the saline perfusion test was 12.59 ng/dL (>10 ng/dL).
Case 3	Remained hypertensive	Normal serum potassium.	The PAC was 20.44 ng/dL after 30 months of follow-up.
Case 4	Remained hypertensive	3.2 mmol/L at one month after surgery; continuous oral potassium supplementation.	The PAC was 18.74 ng/dL after 15 months of follow-up.
Case 5	Remained hypertensive	Normal serum potassium.	The PAC was 21.01 ng/dL after 64 months of follow-up.

PAC, plasma aldosterone concentration; PAC normal value 0.7–15 ng/dL.

ical data.  $P < .05$  was considered statistically significant.

## RESULTS

In our study, 96 patients were diagnosed with APA. Among these, a total of 65 patients underwent partial adrenalectomy and 31 patients underwent total adrenalectomy. Clinical characteristics of APA patients are presented in **Table 1**. No statistical significant differences were observed in gender, tumor site, size of the APA at imaging techniques, preoperative blood pressure levels, serum potassium levels, PAC, ARR, and follow-up time between the 2 groups. Statistical differences were observed in patients' age ( $P = .04$ ).

**Table 2** lists surgical and follow-up results of patients in both groups. Statistical significant differences were observed in operative time ( $P = .01$ ) and number of multiple adenomas ( $P = .01$ ) between the 2 groups. All laparoscopic procedures were successfully performed without conversion to open operations. None of the study subjects showed major intraoperative or postoperative complications, such as injury of adjacent organs or major vessels and long-term supplementation of cortisone.

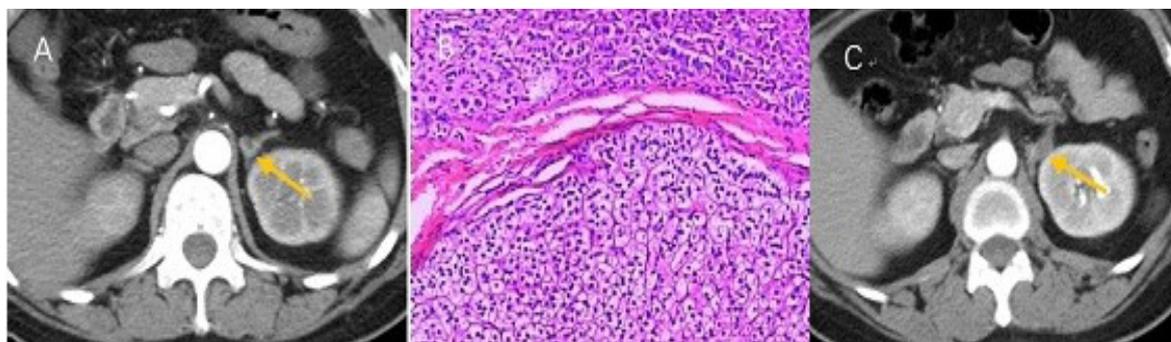
During follow-up, all patients in the laparoscopic total adrenalectomy group showed cure or improvement of hypertension. No patients required potassium supplementation, and plasma aldosterone levels returned to normal levels after surgery. However, in 5 out of 65 patients who underwent laparoscopic partial adrenalectomy, the clinical symptoms of PA failed to improve. None of the 5 patients had improved hypertension, and

3 out of these 5 patients remained hypokalemic and required potassium supplementation. However, the difference in failure of PA between the two groups was not statistically significant. Nevertheless, the failure rate of PA of the laparoscopic partial adrenalectomy group was as high as 7.7%, which was unacceptably high.

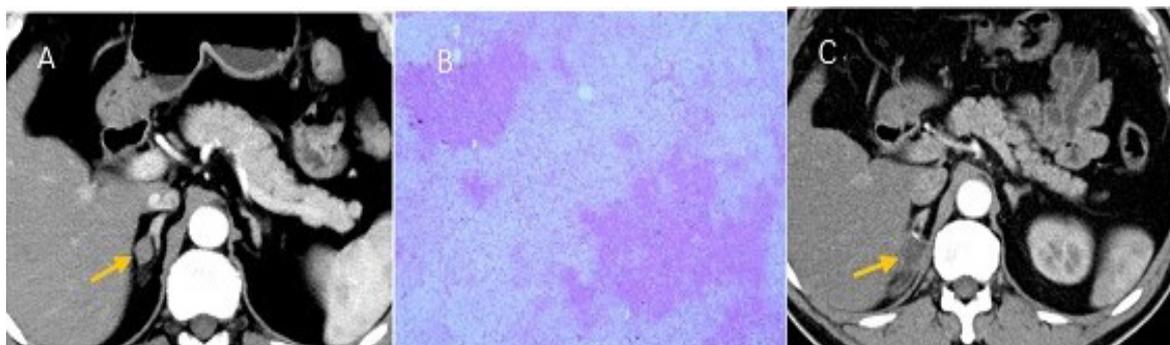
**Table 3** shows the no improvement of PA in 5 APA patients who underwent laparoscopic partial adrenalectomy. These 5 patients remained hypertensive and showed a high PAC after laparoscopic partial adrenalectomy. Moreover, in 3 of 5 patients, serum potassium levels were not normalized after surgery. Furthermore, 2 of 5 patients were followed up with CT, which confirmed tumor recurrence (**Figures 1, 2**). The other 3 patients refused to undergo CT. It is worth mentioning that in a patient it was found that the PAC was 15.21 ng/dL during follow-up, and the plasma aldosterone levels were 12.59 ng/dL ( $> 10$  ng/dL) after the saline infusion test.<sup>(6)</sup> Survival analysis showed no statistically significant difference in postoperative relapse-free survival between the two groups ( $P = .079$ ) (**Figure 3**).

## DISCUSSION

The purpose of this report was to compare the postoperative and follow-up outcomes in 2 groups of APA patients who underwent either laparoscopic partial or total adrenalectomy. With advances in surgical techniques, laparoscopic adrenalectomy has gradually become the gold standard for the treatment of unilateral PA.<sup>(7-9)</sup> However, the method used to cure APA is still controversial, namely laparoscopic partial or total adrenalectomy.



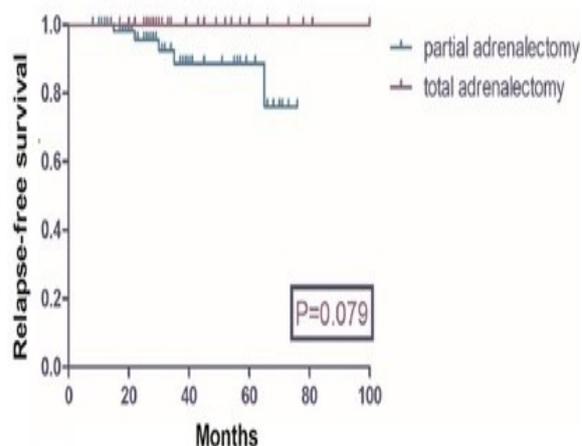
**Figure 1.** **A.** Preoperative computerized tomography (CT) demonstrates unilateral single aldosterone-producing adenoma (APA) (arrow). **B.** Pathological results of the postoperative specimen confirmed as adenoma. **C.** 13 months after surgery, CT showed postoperative tumor recurrence (arrow).



**Figure 2.** A. Preoperative computerized tomography (CT) demonstrates unilateral single aldosterone-producing adenoma (APA) (arrow). B. Pathological results of the postoperative specimen confirmed as adenoma. C. 14 months after surgery, CT showed postoperative tumor recurrence (arrow).

Chen et al. reported that the mean operative time for total adrenalectomy in 47 patients with PA was 103.5 minutes, which is almost consistent with the mean operative time determined in our study (105.33 minutes). However, our findings showed that the time for partial adrenalectomy was shorter compared to the time reported in their study (76.16 vs 95.9 minutes).<sup>(10)</sup> In our study, partial adrenalectomy was performed in younger patients. Probably, the surgeon considered partial adrenalectomy for younger patients to retain more adrenal function. However, if older patients have recurrences after surgery, reoperation may be difficult due to physical conditions. So this may be the reason for the difference in age between the two groups. In addition, both surgical procedures were safe, no significant differences were observed in postoperative recovery, and no major complications occurred intraoperatively or postoperatively.<sup>(7,11,12)</sup>

There are controversies between the two surgical methods. The main reason is that laparoscopic partial adrenalectomy has the advantage of retaining part of the ipsilateral adrenal tissue. However, it also has the disadvantage that the tumor may not be completely removed and residual microadenomas may remain after surgery. Chen,<sup>(10)</sup> Fu,<sup>(11)</sup> and Al-Sobhi<sup>(13)</sup> et al. reported



**Figure 3.** Survival analysis: Comparison of relapse-free survival in postoperative follow-up between the two groups.

Notes: Survival analysis showed no statistically significant difference in postoperative relapse-free survival between the two groups ( $P = .079$ )

the results of 16 and 104 laparoscopic partial adrenalectomies. The average follow-up time was 1 year and 8 years, respectively. None of the patients in their studies had recurrent PA and retained more normal ipsilateral adrenal tissue. In addition, none of the patients' serum cortisol levels were reduced and no exogenous steroid replacement therapy was required after surgery. However, reports on postoperative recurrence of patients with laparoscopic partial adrenalectomy are available. Ishidoya et al. reported that postoperative hypertension and hyperaldosteronism did not improve in 2 out of 29 patients who underwent laparoscopic partial adrenalectomy.<sup>(14)</sup> We performed 65 laparoscopic partial adrenalectomies and experienced 5 cases that did not show improvement of PA after surgery. In 2 of these 5 cases postoperative tumor recurrence was confirmed by CT. In some reports on adrenalectomy in patients with unilateral PA, unilateral single APA was confirmed to account for only 26%-46% by the postoperative pathological results.<sup>(5,15,16)</sup> Although patients were diagnosed by high resolution CT and adrenal vein sampling (AVS) before surgery as unilateral single APA, the postoperative pathological results showed that some patients had multiple adenomas/nodules.<sup>(11,12)</sup> Wiel et al. reported that small adrenal gland micro-nodules were frequently ignored by routine histopathology.<sup>(17)</sup> Using hematoxylin and eosin (HE)-stained sections combined with ex-vivo MRI, macroscopic sections, the pathologist morphologically classified 12 of 15 adrenals as multinodular. In general, partial adrenalectomy may not completely remove microadenomas. Residual microadenomas, which secrete aldosterone may cause PA to fail or recur. In our study, 6 out of 31 patients that underwent total adrenalectomy were pathologically confirmed as multiple adenomas after surgery. Although all patients that underwent partial adrenalectomy were confirmed as APA before and after surgery, 5 out of 65 patients did not improve or relapse, which might confirm the above viewpoint.

Laparoscopic total adrenalectomy is safe and feasible for most adrenal diseases.<sup>(18)</sup> It has fewer perioperative complications and rare postoperative mortality.<sup>(19,20)</sup> In our study, patients who underwent laparoscopic total and partial adrenalectomy did not require cortisol supplementation therapy after surgery. In the partial adrenalectomy group, a total of 5 patients did not achieve improvement of APA, however, all patients in the total adrenalectomy group were cured. No significant differences were observed in surgical outcome between the

two groups, however total adrenalectomy prevented ipsilateral recurrence due to partial adenoma remnants. Although survival analysis showed no statistically significant difference in postoperative relapse-free survival between the two groups ( $P > .05$ ), the  $P$  value was close to a significant level. If the follow-up time is prolonged and the number of cases are increased, there may be statistically significant differences in postoperative recurrence between the two groups.

Our study has several limitations. First, our study is a retrospective study, and the decision criteria for partial or total adrenalectomy procedure were not randomized. Preoperatively, our patients were not selected for AVS, and underwent a CT scan, which might have resulted in diagnostic bias. AVS is an invasive procedure, and if the preoperative imaging scans confirmed unilateral adrenal masses, AVS was not always necessary.<sup>(21-22)</sup> In our study, we have fewer cases of laparoscopic total adrenalectomy and in both total adrenalectomy and partial adrenalectomy, the follow-up time was relatively short. In future studies, we will increase the number of cases and extend the follow-up time.

## CONCLUSIONS

This study showed that laparoscopic partial and total adrenalectomy are technically safe and feasible. However, laparoscopic partial adrenalectomy showed a higher no improvement rate (7.7%) for patients with APA. Therefore, we selected laparoscopic total adrenalectomy for APA patients.

## CONFLICT OF INTEREST

The authors report no conflict of interest.

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