



# Comparison of hand-assisted laparoscopic adrenalectomy vs. laparoscopic adrenalectomy for large pheochromocytomas: a retrospective study

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**Background:** It remains uncertain whether hand-assisted laparoscopic adrenalectomy (HAL) has advantages in treating large pheochromocytomas (PHEOs). This study aimed to assess the feasibility and safety of HAL compared to laparoscopic adrenalectomy (LA).

**Methods:** We conducted a retrospective study on patients with PHEOs  $\geq 6$  cm who received HAL (n=16) and LA (n=20) at Shandong Provincial Hospital from January 2020 to January 2023. The two groups were balanced into 8 pairs using propensity score matching (PSM). Perioperative parameters and long-term follow-up outcomes were compared between the two groups.

**Results:** After adjusting for balance through PSM, patients in the HAL group had shorter operation time (105.00 $\pm$ 18.52 vs. 147.50 $\pm$ 7.07 minutes,  $P<0.001$ ), faster bowel recovery days (1.0 vs. 2.0 days,  $P=0.043$ ), and shorter postoperative hospital stays (5.00 vs. 7.50 days,  $P=0.01$ ). The differences in blood pressure improvement within 3 months postoperatively, and recurrence and metastasis between the two groups (75.00% vs. 62.50%,  $P>0.99$ ; 12.50% vs. 12.50%,  $P>0.99$ ) were not statistically significant.

**Conclusions:** This study suggested that HAL was feasible and safe for patients with large PHEOs. Both HAL and LA showed comparable perioperative and long-term follow-up results.

**Keywords:** Pheochromocytoma (PHEO); perioperative outcomes; hand-assisted; laparoscopic adrenalectomy (LA)

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## Introduction

Pheochromocytomas (PHEOs) are rare neuroendocrine tumors originating in the adrenal medulla, producing catecholamines (1). PHEO is estimated to have an annual incidence rate ranging from two to eight cases per million

individuals (2). The clinical symptoms of PHEOs vary widely, but the most prevalent presentations typically involve paroxysmal or sustained hypertension accompanied by headaches and palpitations (3). PHEO is a condition necessitating prompt diagnosis due to its potential for

severe cardiovascular complications and life-threatening risks (4). For initial screening, evaluating plasma and urinary levels of free norepinephrine and epinephrine stands out as the most accurate method for detecting PHEOs (5,6). Biochemical confirmation of PHEOs is essential prior to proceeding with imaging diagnostics. Anatomical imaging using contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) typically aids in tumor localization.

For adrenal tumors <6 cm, minimally invasive adrenalectomy is the preferred surgical approach (7). Laparoscopic adrenalectomy (LA) is considered as the standard treatment method (8). Compared to open adrenalectomy, LA is associated with reduced blood loss, a shorter postoperative hospital stay, and a more rapid recovery (9,10). Nevertheless, there remains a lack of consensus regarding the efficacy of laparoscopic treatment for large PHEOs (tumors  $\geq 6$  cm). This is probably due to the prolonged duration of surgery, increased blood loss, and instability of the patient's blood flow during the surgical removal of large PHEOs (11). Reportedly, certain large PHEOs, attributed to factors such as tumor adhesion to neighboring structures, have been managed with hand-assisted LA (HAL), deemed a safer, quicker, and more feasible approach (12).

To date, there is still a lack of evidence demonstrating the feasibility of HAL for large PHEOs. As one of the largest urological surgery centers in China specializing in the treatment of adrenal tumors, Shandong Provincial Hospital has accumulated over 5,000 cases of adrenal tumor surgical excision experience. We have discovered substantial

benefits in hand-assisted resection of large PHEOs through our clinical experience, providing a quicker learning curve for trainee adrenal surgeons. Therefore, the aim of this study was to compare the perioperative outcomes and long-term follow-up outcomes of HAL and LA in the treatment of large PHEOs. We present this article in accordance with the STROBE reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/ga-24-407/rc>).

## Methods

### Patients

Totally, 132 patients who underwent surgical resection for PHEOs at Shandong Provincial Hospital from January 2020 to January 2023 entered this retrospective study. All HALs and LAs were performed by Dr. Haiyang Zhang, who had extensive surgical experience in Shandong Provincial Hospital. There were 96 patients excluded from the study due to tumor size <6 cm and missing data. Finally, 36 patients were divided into two groups and included in the final analysis (HAL and LA; *Figure 1*).

### Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Medical Ethics Committee of the Shandong Provincial Hospital Affiliated to Shandong First Medical University (No. 2024-658) and informed consent was taken from all the patients.

### Inclusion and exclusion criteria

The diagnostic criteria for PHEOs in this study included first establishing biochemical evidence of excessive catecholamine secretion by measuring plasma or 24-hour urinary catecholamines and their metabolites. Moreover, imaging techniques like contrast-enhanced CT scans or MRIs of the adrenal glands are conducted to verify the diagnosis of PHEO. All adrenalectomies were performed using HAL or LA. Tumors which had a diameter  $\geq 6$  cm were determined based on the CT or MRI. Postoperative pathology confirmed the diagnosis of PHEOs. Patients with tumor size <6 cm, extra-adrenal PHEOs, bilateral adrenalectomy, advanced clinical stage disease, and absence of postoperative pathology confirming a diagnosis of PHEO were excluded.

### Highlight box

#### Key findings

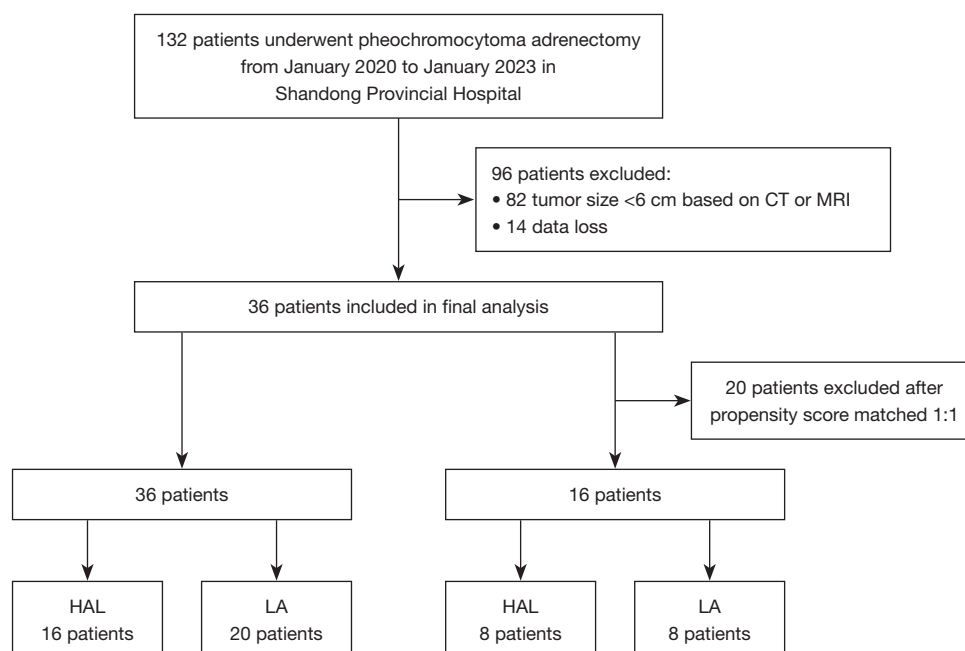
- This study found that hand-assisted laparoscopic adrenalectomy (HAL) was also a viable option for large pheochromocytomas (PHEOs).

#### What is known and what is new?

- Laparoscopic adrenalectomy (LA) is the standard surgical approach for PHEOs.
- HAL is a feasible option for large PHEOs. For large PHEOs, HAL has certain advantages over LA in terms of operative time, postoperative gastrointestinal recovery, and length of hospital stay.

#### What is the implication, and what should change now?

- In clinical practice, for large PHEOs with a high surgical risk, HAL is also a viable option.



**Figure 1** Flow diagram of the study. CT, computed tomography; MRI, magnetic resonance imaging; HAL, hand-assisted laparoscopic adrenalectomy; LA, laparoscopic adrenalectomy.

### Presurgical management

All patients enrolled in this study were treated with an  $\alpha$ -adrenergic receptor blocker for a minimum of 1–2 weeks. Furthermore, they received intravenous infusions of crystalloid and colloid fluids (500–1,000 mL/day) in the 1–2 weeks preceding surgery. Preoperative surgical criteria included blood pressure <130/80 mmHg and heart rate <90 bpm. Before the surgery, we usually assessed the patient's abdominal surface to preliminarily locate the surgical sites for both HAL and LA (Figure 2).

### HAL

The patient was positioned in a jackknife position. For the right-sided tumor, based on preoperative CT imaging (Figure 3A), a hand-assisted device was inserted through a 7 cm vertical incision along the rectus abdominis muscle. A 10 mm trocar was placed 3 cm right of the navel and a 12 mm trocar was placed midline below the rib margin. The dissection technique was similar to fully LA. The non-dominant hand mobilized the colon and liver, creating a working space in the palm and fingers for safe adrenal lesion identification, margin definition, and hepatic flexure, liver, and renal surface dissection (Figure 3B). After the surgery is

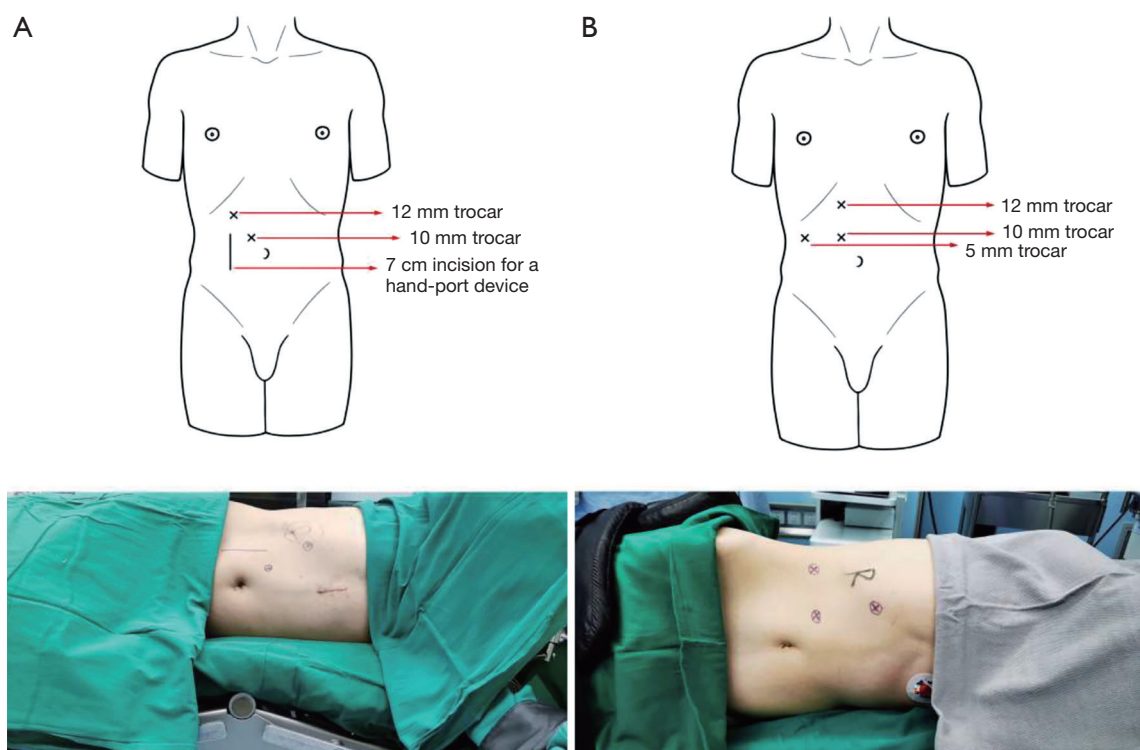
completed and the tumor, along with the adrenal gland, has been entirely removed, the hand-assisted device (Figure 3C) will be the last to be taken out.

### LA

The patient was placed in a jackknife position. A horizontal 1.0 cm incision was made along the midline below the costal margin to insert a 10 mm trocar. A 5 mm trocar was placed at the anterior axillary line and a 12 mm trocar below the costal margin. For the right-sided tumor, a retractor was used to retract the liver, and an ultrasonic scalpel was used to expose the adrenal gland. After tying off the adrenal vessels, the gland was removed for examination.

### Propensity score matching (PSM)

The PSM was used to adjust the differences between the two groups to obtain more precise conclusions. The propensity scores for each patient were determined based on days of using an  $\alpha$ -adrenergic receptor blocker using multivariable logistic regression. The nearest neighbor matching with a caliper width of 0.1 was employed for both HAL and LA, with a 1:1 matching ratio in PSM.



**Figure 2** The placement of the hand-assisted device and the patient's jackknife position. (A) HAL. (B) LA. HAL, hand-assisted laparoscopic adrenalectomy; LA, laparoscopic adrenalectomy.

### *Follow-up protocol after surgery*

After surgery, patients would attend their first follow-up appointment within 2 to 6 weeks. Following that, we usually assess them every 3 months to monitor blood pressure improvements and look for any signs of recurrence or complications. Catecholamine levels in both plasma and urine are measured at 3 months, 6 months, and then annually thereafter. If any indications of recurrence arise, particularly with abnormal biochemical markers, we may carry out imaging studies such as MRI, CT, or positron emission tomography (PET)-CT scans.

### *Variables*

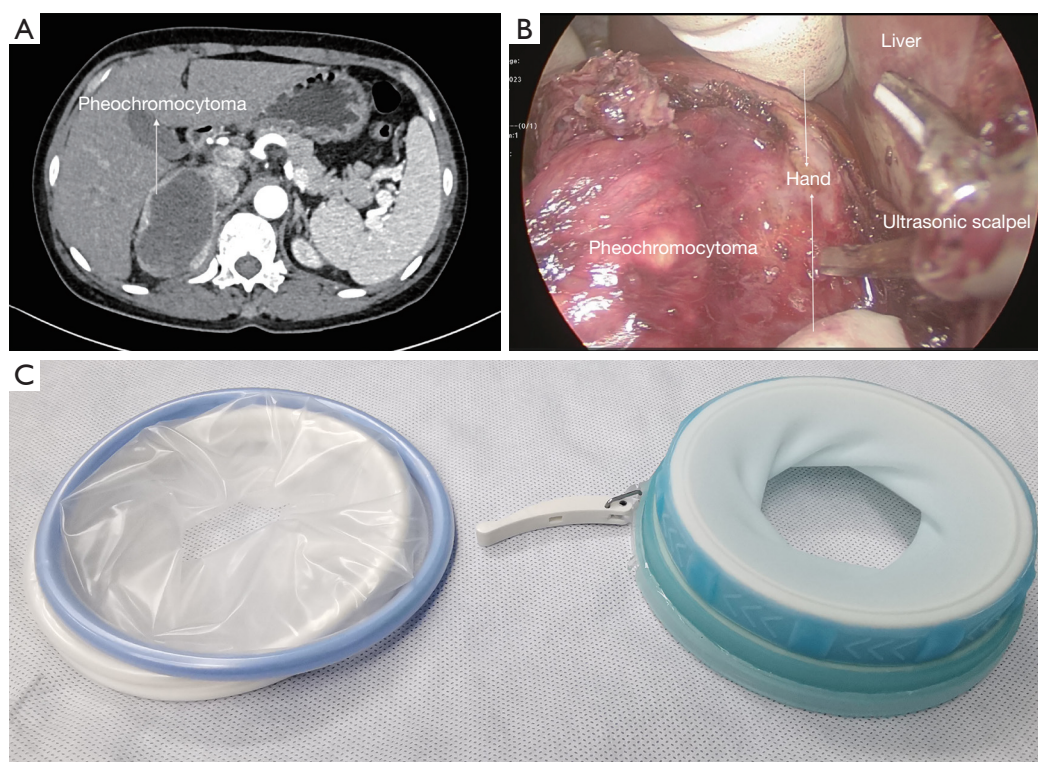
The demographic characteristics of the two patient groups were compared, which included age, gender, body mass index (BMI), hypertension, comorbidities (diabetes, coronary artery disease, heart attack, stroke), tumor side, tumor size, American Society of Anesthesiologists Physical Status Classification System (ASA) score (13,14), duration of  $\alpha$ -adrenergic receptor blocker use, and duration of

intravenous crystal/colloid fluid administration. The perioperative outcomes of both groups were analyzed. The intraoperative data encompassed operation time, anesthesia duration, estimated blood loss, transfusion rate, decrease in hemoglobin, and intraoperative hemodynamic parameters. Postoperative data included bowel recovery, duration of hospital stay after surgery, transfusion rate, intraperitoneal drainage on the first postoperative day, and any postoperative complications. Long-term follow-up data included postoperative blood pressure improvement within 3 months, and recurrence and metastasis rates.

### *Statistical analysis*

All data were processed and analyzed using SPSS version 27.0. Continuous variables with a normal distribution were reported as mean  $\pm$  standard deviation. For non-normally distributed continuous variables, the median (interquartile range) was used. Categorical variables were presented as count (percentage). The independent sample Student's *t*-test was employed to compare the means of two normally distributed continuous variables, while the Mann-





**Figure 3** Surgical data for a patient with PHEO. (A) Preoperative CT imaging examination. (B) Dissection of a right-sided adrenal tumor located below the liver. (C) The hand-assist device. PHEO, pheochromocytoma; CT, computed tomography.

Whitney *U* test was used for non-normally distributed continuous variables. Categorical variables were analyzed using Pearson's Chi-squared test or Fisher's exact test. The recurrence-free rate and survival rate were determined using Kaplan-Meier curves and assessed with log-rank tests.

## Results

In the final analysis, 36 patients were included and divided into two groups: 16 patients in the HAL group and 20 patients in the LA group. After PSM, a balance in baseline variables was attained between the two groups. Specifically, 16 patients who received HAL were matched with 20 patients who received LA, resulting in eight pairs with similar characteristics.

Prior to PSM, the only baseline variable imbalance between the HAL group and the LA group was observed in the duration of  $\alpha$ -adrenergic receptor blocker use [7.50 (5.00–10.00) *vs.* 10.50 (7.00–12.00), *P*=0.047]. After adjusting for variables using PSM, balance was achieved with no significant difference [6.00 (5.00–7.75) *vs.* 6.00

(5.00–7.75), *P*>0.99]. The preoperative indicators showed no statistically significant differences in both groups before and after PSM (*Table 1*). The revised sentence: In the PSM-adjusted cohort, the mean ages of patients in the HAL and LA groups were 52.50 (44.00–64.75) and 49.50 (37.75–69.00) years, respectively. The majority of patients were male (50.00% *vs.* 62.50%). The BMI was  $24.76 \pm 3.83$  and  $21.52 \pm 2.93$  kg/m<sup>2</sup>, and the percentage of patients with hypertension at admission was 37.50% and 62.50% in the HAL and LA groups. The average tumor sizes were 8.45 and 6.25 cm for the HAL and LA groups, and the preoperative days of fluid supplementation were 7.75 and 5.00 days. Most patients in both groups had high ASA scores [3–4], with percentages of 75.00% and 100.00%, respectively.

*Table 2* displays the perioperative results. There were no statistically significant variances observed in estimated blood loss (50.00 *vs.* 55.00 mL), intraoperative transfusion rate (0.00% *vs.* 12.50%), and hemoglobin decline (10.00 *vs.* 13.50 g/L) between the two groups. Moreover, the hemodynamic parameters during the surgery were comparable in both groups, with no statistically significant

**Table 1** Demographics and pre-operative data of patients

Variables	Before PSM			After PSM		
	HAL (n=16)	LA (n=20)	P	HAL (n=8)	LA (n=8)	P
Age (years)	45.00 (32.00–58.00)	52.00 (40.00–63.00)	0.31	52.50 (44.00–64.75)	49.50 (37.75–69.00)	0.94
Sex			0.55			>0.99 <sup>†</sup>
Male	8 (50.00)	12 (60.00)		4 (50.00)	5 (62.50)	
Female	8 (50.00)	8 (40.00)		4 (50.00)	3 (37.50)	
BMI (kg/m <sup>2</sup> )	23.72 (20.94–24.54)	23.01 (19.38–25.44)	0.50	24.76±3.83	21.52±2.93	0.08
Hypertension at admission	5 (31.25)	9 (45.00)	0.40 <sup>†</sup>	3 (37.50)	5 (62.50)	0.62 <sup>†</sup>
History of hypertension	14 (87.50)	18 (90.00)	>0.99 <sup>†</sup>	7 (87.50)	7 (87.50)	>0.99 <sup>†</sup>
Comorbidities						
Diabetes mellitus	8 (50.00)	9 (45.00)	0.77	6 (75.00)	4 (50.00)	0.61 <sup>†</sup>
Coronary heart disease	3 (18.75)	4 (20.00)	0.70 <sup>†</sup>	3 (37.50)	0 (0.00)	0.20 <sup>†</sup>
Heart attack	3 (18.75)	2 (10.00)	0.64 <sup>†</sup>	1 (12.50)	0 (0.00)	>0.99 <sup>†</sup>
Stroke	3 (18.75)	3 (15.00)	>0.99 <sup>†</sup>	1 (12.50)	1 (0.00)	>0.99 <sup>†</sup>
Tumor size (cm)	6.90 (6.00–10.00)	6.50 (6.00–7.82)	0.39	8.45 (6.00–14.00)	6.25 (6.00–6.65)	0.17
Tumor side			0.20			>0.99 <sup>†</sup>
Left	9 (56.25)	7 (35.00)		3 (37.50)	4 (50.00)	
Right	7 (43.75)	13 (65.00)		5 (62.50)	4 (50.00)	
Duration of $\alpha$ -adrenergic receptor blocker use (days)	7.50 (5.00–10.00)	10.50 (7.00–12.00)	0.047	6.00 (5.00–7.75)	6.00 (5.00–7.75)	>0.99
Duration of intravenous crystal/colloid fluid administration (days)	8.75±2.70	8.90±4.49	0.90	7.75±2.71	5.00±2.67	0.06
ASA score			0.57 <sup>†</sup>			0.46 <sup>†</sup>
1/2	2 (12.50)	1 (5.00)		2 (25.00)	0 (0.00)	
3/4	14 (87.50)	19 (95.00)		6 (75.00)	8 (100.00)	

Data are presented as mean  $\pm$  standard deviation, median (IQR), or n (%). <sup>†</sup>, Fisher's exact test. PSM, propensity score matching; HAL, hand-assisted laparoscopic adrenalectomy; LA, laparoscopic adrenalectomy; BMI, body mass index; ASA, American Society of Anesthesiologists Physical Status Classification System; IQR, interquartile range.

distinctions. The HAL group demonstrated a shorter operation duration (105.00±18.52 *vs.* 147.50±7.07 minutes,  $P<0.001$ ), quicker bowel recovery time (1.0 *vs.* 2.0 days,  $P=0.043$ ), and briefer postoperative hospital stays (5.00 *vs.* 7.50 days,  $P=0.01$ ) compared to the LA group. Both groups exhibited similar outcomes in terms of postoperative blood pressure improvement within 3 months, and recurrence and metastasis. After long-term follow-up, the recurrence-free rate ( $P=0.89$ ) and survival rate ( $P=0.36$ ) between the HAL and LA groups were comparable (*Figure 4*).

Postoperative complications between the two groups,

including incision infection, peritonitis, short-term intestinal obstruction, renal atrophy and anemia were compared. The incidence rates of postoperative complications in both groups were low and showed no statistically significant differences.

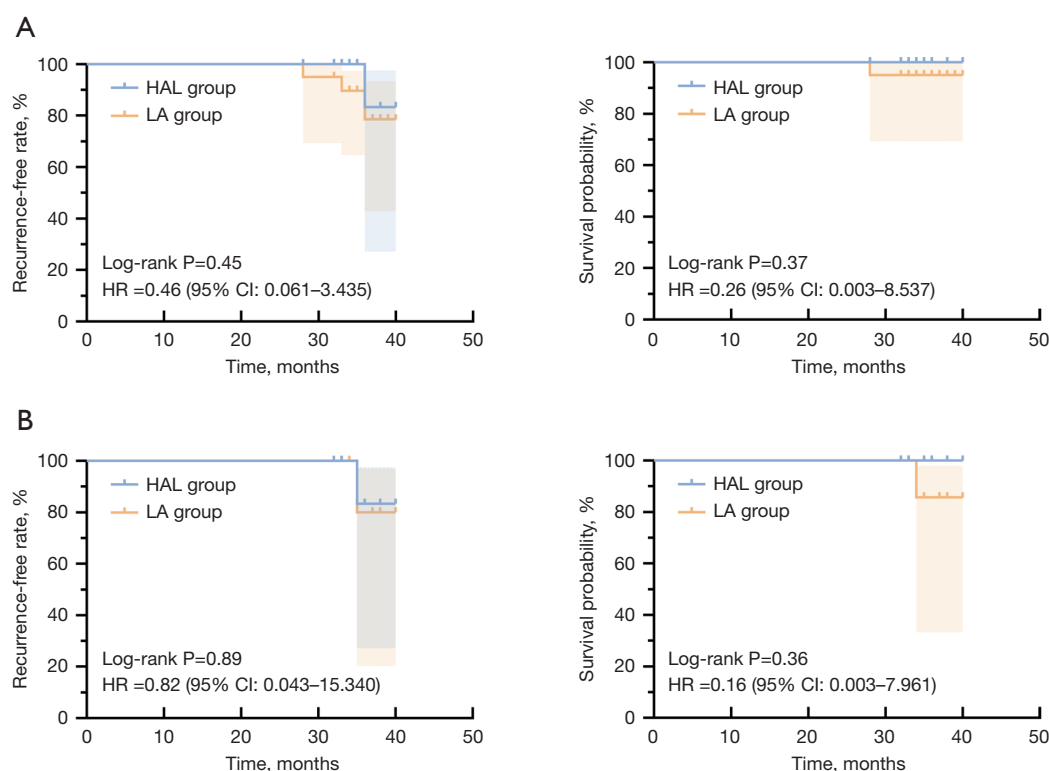
## Discussion

The anatomical structure and biochemical properties of the adrenal glands contribute to the complexity and high-risk nature of adrenal surgery in the field of urology (15,16).

**Table 2** Perioperative and prognostic data of patients

Variables	Before PSM			After PSM		
	HAL (n=16)	LA (n=20)	P	HAL (n=8)	LA (n=8)	P
<b>Intraoperative data</b>						
Operating time (minutes)	106.88±15.26	147.50±15.52	<0.001	105.00±18.52	147.50±7.07	<0.001
Estimated blood loss (mL)	55.00 (50.00–100.00)	90.00 (50.00–100.00)	0.09	50.00 (50.00–57.50)	55.00 (50.00–100.00)	0.27
Transfusion	0 (0.00)	3 (15.00)	0.24 <sup>†</sup>	0 (0.00)	1 (12.50)	>0.99 <sup>†</sup>
Decrease in hemoglobin (g/L)	10.00 (9.00–15.75)	14.50 (8.50–25.00)	0.20	10.00 (9.25–15.75)	13.50 (6.75–22.00)	0.34
Maximum SBP (mmHg)	175.31±16.98	172.00±18.81	0.59	180.63±16.35	167.50±12.82	0.10
Minimum SBP (mmHg)	105.00 (90.00–115.00)	100.00 (90.00–110.00)	0.20	107.50 (90.00–115.00)	105.00 (100.00–110.00)	0.91
Systolic instability	60.00 (50.00–90.00)	60 (60.00–92.50)	0.41	60.00 (60.00–105.00)	60.00 (52.50–70.00)	0.44
SBP >200 mmHg	2 (12.50)	2 (10.00)	>0.99 <sup>†</sup>	2 (25.00)	0 (0.00)	0.47 <sup>†</sup>
SBP >160 mmHg	11 (68.75)	16 (80.00)	0.47 <sup>†</sup>	7 (87.50)	6 (75.00)	>0.99 <sup>†</sup>
Maximum DBP (mmHg)	90.00 (85.00–90.00)	90.00 (90.00–100.00)	0.27	90.00 (80.00–105.00)	90.00 (82.50–97.50)	0.91
Minimum DBP (mmHg)	60.00 (50.00–70.00)	50.00 (50.00–60.00)	0.23	65.00 (50.00–70.00)	50.00 (50.00–50.00)	0.09
Diastolic instability	32.50 (17.50–52.50)	40.00 (32.50–40.00)	0.45	25.00 (10.00–57.50)	40.00 (32.50–40.00)	0.42
Heart rate >110 bpm	5 (31.25)	9 (45.00)	0.40	3 (37.50)	3 (37.50)	>0.99 <sup>†</sup>
<b>Postoperative data</b>						
Bowel recovery (days)	1.00 (1.00–1.00)	2.00 (1.00–2.75)	0.002	1.00 (1.00–1.00)	2.00 (1.00–2.75)	0.043
Duration of postoperative hospital stay (days)	6.00 (5.00–6.00)	7.00 (6.00–8.00)	0.002	5.00 (5.00–6.00)	7.50 (6.25–8.00)	0.01
Transfusion	3 (18.75)	5 (25.00)	0.71 <sup>†</sup>	1 (12.50)	2 (25.00)	>0.99 <sup>†</sup>
Intraperitoneal drainage on the first day after surgery (mL)	70.00 (50.00–100.00)	50.00 (22.50–70.00)	0.10	60.00 (50.00–100.00)	60.00 (27.50–92.50)	0.79
Incision infection	1 (6.25)	0 (0.00)	0.44 <sup>†</sup>	1 (12.50)	0 (0.00)	>0.99 <sup>†</sup>
Peritonitis	0 (0.00)	1 (5.00)	>0.99 <sup>†</sup>	0 (0.00)	1 (12.50)	>0.99 <sup>†</sup>
Renal atrophy	0 (0.00)	1 (5.00)	>0.99 <sup>†</sup>	0 (0.00)	1 (12.50)	>0.99 <sup>†</sup>
Anemia	2 (12.50)	6 (30.00)	0.26 <sup>†</sup>	2 (25.00)	4 (50.00)	0.61 <sup>†</sup>
Short-term intestinal obstruction	1 (6.25)	3 (15.00)	0.61 <sup>†</sup>	1 (12.50)	2 (25.00)	>0.99 <sup>†</sup>
<b>Follow-up data</b>						
Follow-up time (months)	34.75±2.79	34.95±2.74	0.83	35.50±2.45	35.75±2.38	0.84
Blood pressure improved within 3 months	13 (81.25)	16 (80.00)	>0.99 <sup>†</sup>	6 (75.00)	5 (62.50)	>0.99 <sup>†</sup>
Recurrence and metastasis	1 (6.25)	2 (10.00)	>0.99 <sup>†</sup>	1 (12.50)	1 (12.50)	>0.99 <sup>†</sup>

Data are presented as mean ± standard deviation, median (IQR), or n (%). <sup>†</sup>, Fisher's exact test. PSM, propensity score matching; HAL, hand-assisted laparoscopic adrenalectomy; LA, laparoscopic adrenalectomy; SBP, systolic blood pressure; DBP, diastolic blood pressure; IQR, interquartile range.



**Figure 4** The recurrence-free rate and survival of the HAL and LA groups. (A) Before PSM. (B) After PSM. HAL, hand-assisted laparoscopic adrenalectomy; LA, laparoscopic adrenalectomy; HR, hazard ratio; CI, confidence interval; PSM, propensity score matching.

Since its introduction by Gagner in 1992, LA has emerged as the common procedure for adrenal tumors (17). LA for PHEOs poses greater challenges compared to other adrenal tumors, given the significant intraoperative blood pressure fluctuations commonly observed, particularly in cases of large PHEOs (18–20). Recent studies have indicated that HAL may offer advantages over traditional LA for the management of large PHEOs (12,21). The rarity of large PHEOs poses challenges for conducting randomized clinical trials within a constrained timeframe. Therefore, a retrospective analysis was conducted in the present study to compare HAL and LA in treating large PHEOs.

The data of patients with PHEOs  $\geq 6$  cm over the past 3 years in Shandong Provincial Hospital were retrospectively reviewed. We obtained more reliable conclusions by utilizing PSM to mitigate baseline imbalances. Following PSM adjustment, the results demonstrated that HAL had shorter operation time, hospital stay, and bowel recovery days. Since Bennett's first report in 2002 (22), HAL has been studied and widely applied. In 2002, Bennett first utilized HAL for treating adrenal tumors, but their study only

included three cases of small-sized tumors (1.0–2.7 cm). In their research, HAL did not show significant advantages compared to LA. The challenges of traditional LA in treating large PHEOs include the risk of organ damage due to adhesions, significant bleeding, severe blood pressure fluctuations, and prolonged surgical durations (23). Using a hand-port device, HAL provides the advantages of minimally invasive surgery and safety with tactile feedback. The average operation time for HAL was shorter, with less interference with organs such as the gastrointestinal tract and minimal occurrence of organ dysfunction. This could clarify why patients with HAL needed less time to resume oral intake and had shorter hospital stays. Although the average hospital stay for LAs is 1–2 days, our study involving large PHEOs showed a relatively long postoperative recovery period. This extended hospital stay can be attributed to several factors: the large tumor size (average diameter  $\geq 6$  cm), increased intraoperative blood loss, prolonged surgical time, and the occurrence of postoperative complications such as short-term bowel obstruction and anemia. Furthermore, the underlying health



conditions and age of certain patients also contributed to the extended recovery period.

Intraoperative hemodynamic instability (IHD) is crucial for patients' recovery after surgery (24). IHD presents a major surgical and anesthetic challenge during PHEOs resection and has been shown to be a significant independent risk factor for cardiovascular-specific complications (25). In the study, there were no statistically significant differences in hemodynamics-related indicators between the HAL and LA groups. There were no statistically significant differences in postoperative complications between the two groups, indicating that HAL and LA had similarly low rates of complications. It is worth noting that one patient in the LA group suffered from severe postoperative renal atrophy in this study.

Renal atrophy may be caused by damage to the renal hilum nerves and renal vascular adventitia during surgery, even without any rupture of the renal artery and vein. Additionally, scarring in the surgical site may also put pressure on the renal hilum vessels, resulting in renal artery stenosis and subsequent renal atrophy. Furthermore, significant improvements in blood pressure in both groups were observed within 3 months, although there was no statistically significant difference between the two groups. In our study, we found a low rate of postoperative peritonitis, reporting just one case in the LA group. This patient exhibited symptoms such as abdominal pain, fever, and nausea, along with vomiting, and was managed with antibiotics and nutritional support. The HAL group recorded one case of recurrence and metastasis, whereas the LA group had two cases. During postoperative follow-up in the HAL group, a patient was discovered to have developed a new tumor in the tumor bed. In the LA group, one patient was identified with a liver tumor, suggesting possible metastasis, while another patient, who sought treatment for bone pain, was diagnosed with bone metastasis. All surgical margins were negative in our cohort. Both groups exhibited relatively low rates of recurrence and metastasis following surgery. The survival curves showed comparable outcomes in terms of recurrence-free rate and survival rate between the HAL and LA groups both before and after PSM adjustment. Collectively, these data indicated that HAL was a safe and effective strategy for treating PHEOs.

Our results were consistent with another retrospective analysis (21). However, their study lacked a comparison between HAL and LA, had small adrenal tumor volumes, and did not have long-term follow-up results. Most

importantly, their study focused on large adrenal tumors rather than PHEOs. Expanding on this groundwork, our study focused on large PHEOs, a subgroup with scarce comparative data. We observed that both procedures yielded satisfactory intraoperative and postoperative results. Moreover, our investigation underscored nuanced distinctions between HAL and LA, notably in terms of tactile feedback, surgical duration, and postoperative recuperation. This showcased the superiority of HAL over LA, offering crucial insights for surgical decision-making in this patient cohort.

Before concluding, some factors need to be carefully considered. Firstly, this was a selective retrospective analysis, although PSM improved the reliability of the conclusions. Secondly, the perioperative data were obtained from anesthesia record sheets, which were updated every 5 minutes. The potential lack of accuracy may have an impact on the conclusions. Thirdly, due to the low incidence of the disease, the sample size of patients included in this study is limited. The limited sample size may influence the reliability and generalizability of our results. Therefore, future research should involve a larger patient population to confirm our findings, and prospective studies are still needed for further validation. Moreover, due to the limitations of Shandong Provincial Hospital's pathology results, which are unable to effectively use current scoring systems to predict the malignant potential of tumors, we cannot fully assess the risk of tumor metastasis. In addition, some specialists may perceive the 7 cm incision in HAL as quite significant. However, our considerable experience has shown that HAL provides notable benefits, especially in the management of large PHEOs. Importantly, in the case of large PHEOs, a considerable incision is still necessary after LA to ensure the entire tumor is removed.

## Conclusions

In conclusion, for patients with large PHEOs, HAL was found to be feasible, safe, and could potentially be utilized as an alternative to laparoscopy in certain high-risk surgeries.

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## Footnote

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**Ethical Statement:** The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Medical Ethics Committee of the Shandong Provincial Hospital Affiliated to Shandong First Medical University (No. 2024-658) and informed consent was taken from all the patients.

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