

Original Research

Comparison of transperitoneal laparoscopic versus open adrenalectomy for large pheochromocytoma: A retrospective propensity score-matched cohort study

Song Bai, Zichuan Yao, Xianqing Zhu, Zidong Li, Yunzhong Jiang, Rongzhi Wang, Bin Wu*

Department of Urology, Shengjing Hospital of China Medical University, Shenyang 110004, China

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ABSTRACT

Background: Surgical resection is the main treatment strategy for pheochromocytoma. Whether laparoscopic techniques are feasible for large pheochromocytoma treatments is controversial. The aim of this study was to evaluate the feasibility and safety of transperitoneal laparoscopic adrenalectomy (LA) compared with open adrenalectomy (OA).

Methods: We retrospectively studied 182 patients with radiographic tumor sizes ≥ 6 cm who underwent adrenalectomy at our center between 1 January 2007 and 31 December 2017. After propensity score-matching to balance baseline variables, 82 patients treated with LA and 100 patients treated with OA were grouped into 64 pairs. Patient demographics, and extensive peri-operative and oncologic data were recorded and compared.

Results: In the matched group, the incidence of intra-operative hemodynamic instability, transfusion rate, prolonged hypotension, and cardiovascular morbidity in the LA group were lower than the OA group (25.0% vs. 48.4%, 29.7% vs. 46.9%, 4.7% vs. 23.4%, and 14.1% vs. 37.5%, respectively). The estimated blood loss was less (100 ml vs. 300 ml) and bowel recovery was quicker (1.9 d vs. 2.3 d) in the LA group. The proportion of patients in whom blood pressure returned to normal ($P = 0.184$), had recurrences ($P = 0.197$), and survived ($P = 0.763$) were equivalent. The surgical approach (OA vs. LA) was an independent risk factor for IHD, prolonged hypotension, cardiovascular morbidity, and longer bowel recovery.

Conclusions: This propensity score-matched cohort study showed that LA was feasible, safe, and superior to OA for patients with large pheochromocytoma, meanwhile LA had comparable oncological outcomes compared with OA after a lengthy follow-up.

1. Introduction

Pheochromocytoma are rare neuroendocrine tumors that originate from the adrenal medulla. Surgical resection is the main treatment strategy [1]. Despite widespread application of pre-operative medical preparation, and improvement in anesthetic and surgical techniques, morbidity and mortality are still common because of the fluctuation in catecholamine levels peri-operatively [2–4].

Large pheochromocytoma (radiographic tumor size ≥ 6 cm) are more challenging to manage because of the significant association with intra-operative hemodynamic instability (IHD) and severe morbidity compared with smaller pheochromocytoma (< 6 cm) [2]. Open adrenalectomy (OA) is the most common strategy for large pheochromocytoma because of the wide surgical field; however, the complex anatomy, rich vascularity of the tumor, and higher incidence of IHD

remain a challenge for the surgeon [5]. Laparoscopic adrenalectomy (LA) is the standard treatment modality for small adrenal tumor (< 6 cm) and is widely accepted because of minimally invasive access, fine dissection capability, and a clear operative field compared with the open approach [6].

Whether the LA technique is feasible for large pheochromocytoma is controversial because no randomized controlled trials and limited retrospective studies have addressed this issue. Indeed, there is an urgent need to collect evidence to help reach an objective conclusion regarding the surgical management of large pheochromocytoma. The aim of this retrospective score-matched study was to evaluate the feasibility and safety of transperitoneal LA compared with OA.

* Corresponding author. Department of Urology, Shengjing Hospital of China Medical University, 36 Sanhao Street, Shenyang, Liaoning, 110004, China.

E-mail addresses: bais@sj-hospital.org (S. Bai), 17612491522@163.com (Z. Yao), 18302427176@163.com (X. Zhu), andy901203@outlook.com (Z. Li), 18304095870@163.com (Y. Jiang), baisongcmu@163.com, rongzhi_wang@yahoo.com (B. Wu).

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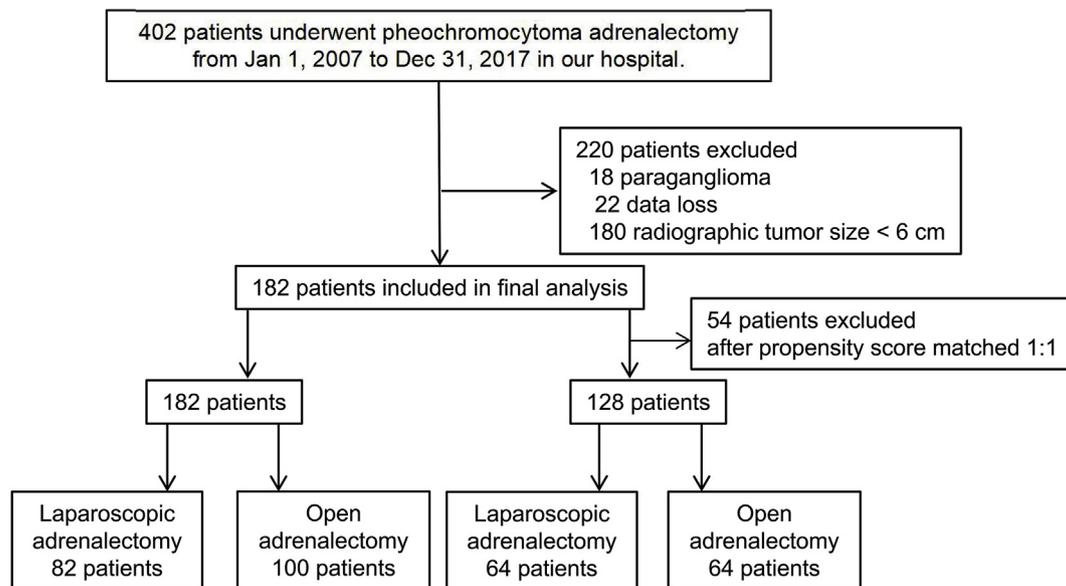


Fig. 1. Flow diagram of the study.

2. Methods

2.1. Patients

We retrospectively studied 402 patients who underwent surgical resection of pheochromocytoma at our center between 1 January 2007 and 31 December 2017. Two hundred twenty patients were excluded from the study because of ectopic pheochromocytoma, missing data, or radiographic tumor size < 6 cm. One hundred eighty-two patients were included in the final analyses, and divided into two groups (transperitoneal LA and OA; Fig. 1).

This study has been reported in line with the STROCSS criteria [7]. Chinese Clinical Trial Registry (ChiCTR) website: <http://www.chictr.org.cn/index.aspx>, registration number is ChiCTR1800017847. Ethics Committee No. Is 2018PS398K.

2.2. Inclusion and exclusion criteria

The diagnosis of pheochromocytoma was confirmed by pathological examinations. All unilateral adrenalectomy undergone by transperitoneal laparoscopy or open approaches were included. The clinical stage was localized disease. The American Society of Anesthesiologists (ASA) scores were 1–4 [6,8]. The tumor size was ≥ 6 cm based on computer tomography. Patients who underwent bilateral adrenalectomy or ectopic pheochromocytoma were excluded.

2.3. Propensity score-matching

We used the propensity score-matching (PSM) method to adjust the baseline differences between the LA and OA groups in an effort to derive more accurate conclusions. Multivariate logistic regression was used to determine propensity scores for each patient based on age, sex, body mass index (BMI), the ASA score, radiographic tumor size, hypertension comorbidity, and use of an α -adrenoreceptor antagonist pre-operatively, which were demographics or unbalanced variables before PSM between the two groups LA and OA were matched 1:1 using a caliper width of 0.1 for the propensity score through nearest neighbor matching. We achieved a balance between the LA and OA groups after PSM; 82 patients treated with LA and 100 patients treated with OA were balanced into 64 pairs (Fig. 2).

2.4. Pre-operative preparation

In our institution, some patients who had typical biochemical and radiographical manifestations of pheochromocytoma were treated with doxazosin, terazosin, or prazosin at least 2 weeks pre-operatively. Some patients who had malignant hypertension or larger tumors were admitted for intravenous crystal/colloid (2000 ml/day) fluids or blood transfusion 2–3 d before surgery. The criteria for pre-operative medical preparation included a blood pressure < 130/80 mmHg, heart rate < 90/min, and hematocrit < 0.45.

2.5. Surgical technique for transperitoneal LA

The patient was placed in the lateral decubitus position. The first port was inserted through an incision 2 cm below and parallel to the costal margin and near the midclavicular line. Three additional trocars were positioned below and around the tumor in a sector distribution under direct visualization. The pneumoperitoneum pressure was 12–15 mmHg. First, we mobilized the right lobe of the liver for right-sided tumors or the spleen and the pancreatic tail for left-sided tumors, exposed the adrenal tumor, then the main adrenal vein was double-clipped using a Hem-o-lock® after the tumor was dissected from the adjacent structures. The tumor was placed in a bag and removed *en bloc* through first trocar site.

2.6. Surgical technique for OA

The patient was placed in the supine position with a subcostal incision length appropriate for the tumor size. First, we mobilized the right lobe of the liver for right-sided tumors or the spleen and pancreatic tail for left-sided tumors and dissected the medial and lateral attachments of the tumor. The adrenal vein was subsequently exposed at the inferior margin of the left adrenal or the medial margin of the right adrenal, then the adrenal vein was double-ligated. The specimen was removed *en bloc* after the tumor had been completely isolated.

2.7. Outcome and follow-up

Patient demographics (sex, age, and BMI), comorbidity (ASA score, diabetes mellitus [DM], coronary heart disease [CHD], hypertension, and arrhythmias), disease characteristics (tumor side and radiographic tumor size), extensive pre-operative (use of an α -adrenoreceptor

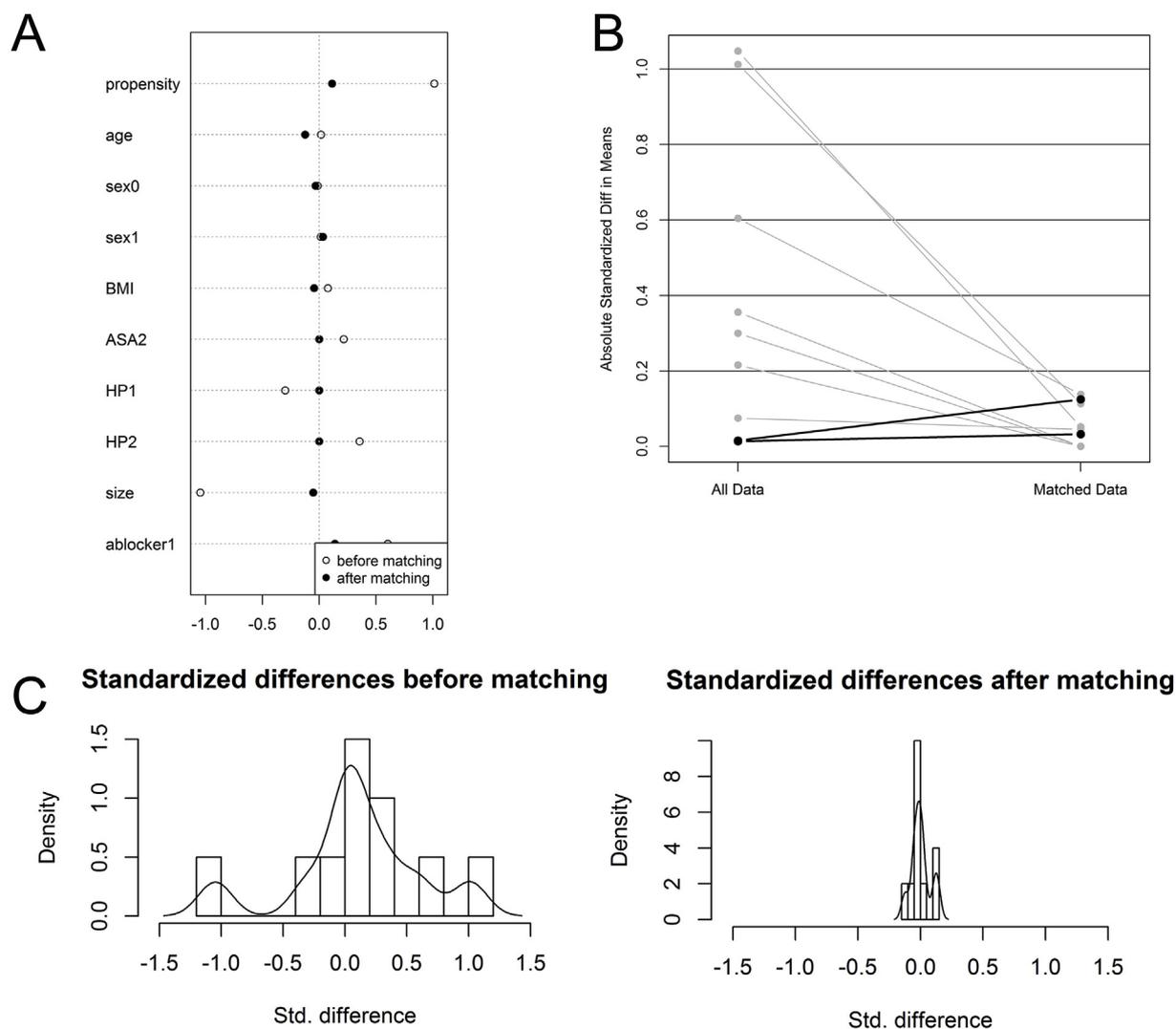


Fig. 2. Plot of the propensity score-matched study. A: dot plot of standardized mean difference, B: line plot of individual differences, C: histogram of standardized mean differences (before and after).

antagonist, blood transfusion, and 24-h urine vanillylmandelic acid [VMA] level), intra-operative factors (duration of surgery, IHD, estimated blood loss, and blood transfusion rate), and post-operative factors (time to bowel recovery, length of hospital stay, prolonged hypotension, blood transfusion rate, morbidity, and normalization of blood pressure), and oncological data (recurrence and survival rates) were recorded.

Morbidity was classified according to the Clavien-Dindo classification [10]. Severe morbidity was defined as Clavien II and greater. Cardiovascular morbidity was defined as complications related to the cardiovascular system, such as prolonged post-operative hypotension requiring norepinephrine or need for blood transfusion, myocardial ischemia, stroke, ventricular fibrillation, and pulmonary embolism/deep vein thrombosis. The definition of IHD was the presence of at least one intra-operative systolic blood pressure reading (SBP) > 200 mmHg or a mean arterial pressure (MAP) < 60 mm Hg requiring norepinephrine or a blood transfusion for maintaining normal blood pressure intra-operatively [9]. Prolonged hypotension was defined as a MAP < 60 mmHg or requiring norepinephrine or blood transfusion for maintaining normal blood pressure post-operatively. Follow-up data were obtained through telephone calls and office visits for blood pressure readings and oncology data at our institution.

2.8. Statistical analysis

Continuous variables with a normal distribution were reported as the mean ± standard deviation (SD). Non-normal continuous variables were expressed as the median (interquartile range). Categorical variables were reported as the number (percentage). An independent sample Student's *t*-test was used to compare the means of two continuous normally distributed variables and the Mann-Whitney *U* test was applied to compare the means of two continuous non-normally distributed variables. Pearson's chi-square test or Fisher's exact test was used for categorical variables. Recurrence and survival rates were calculated using Kaplan-Meier curves with a log-rank test. The adjusted odds ratio (OR) and 95% confidence interval (CI) were determined by binary logistic regression and the β coefficient was calculated by multiple linear regression. Statistical analyses were performed using SPSS 22.0 for Windows (SPSS, Inc., Chicago, IL, USA). Values of *P* < 0.05 (two-tailed) were considered statistically significant.

3. Results

There were 182 patients included in the final analysis, and divided into two groups (transperitoneal LA [82 patients] and OA [100 patients]). We achieved a balance of baseline variables between the two groups after PSM; 82 patients treated with LA and 100 patients treated

Table 1
Demographics and pre-operative data of patients undergoing pheochromocytoma adrenalectomy in this cohort.

Variable	Propensity before 182 patients			Propensity after 128 patients		
	LA	OA	P value	LA	OA	P value
Number of patients (%)	82 (100)	100 (100)		64 (100)	64 (100)	
Follow up period, months	38.0 (16.0–60.0)	73.0 (47.0–106.0)		36.0 (12.5–36.0)	65 (34.5–91.5)	
Demographic characteristics						
Mean age (years)	51.4 ± 13.1	51.2 ± 12.8	0.916	51.9 ± 13.3	51.7 ± 13.4	0.937
Sex female	47 (57.3)	58 (58.0)	0.478	37 (57.8)	33 (51.6)	0.478
male	35 (42.7)	42 (42.0)		27 (42.2)	31 (48.4)	
BMI (kg/m ²)	23.4 (20.6–25.1)	22.8 (20.0–25.3)	0.587&	23.4 (20.4–25.1)	23.1 (20.2–26.1)	0.888&
Comorbidities						
ASA score 0/1/2	63 (76.8)	86 (86.0)	0.110	51 (79.7)	53 (82.8)	0.651
3/4	19 (23.2)	14 (14.0)		13 (20.3)	11 (17.2)	
Coronary heart disease	23 (28.0)	38 (38.0)	0.157	18 (28.1)	22 (34.4)	0.446
Hypertension normal	33 (40.2)	43 (43.0)	0.017	27 (42.2)	21 (32.8)	0.339
continuous	24 (29.3)	43 (43.0)		21 (32.8)	29 (45.3)	
intermittent	25 (30.5)	14 (14.0)		16 (20.5)	14 (21.9)	
Arrhythmia	6 (7.3)	3 (3.0)	0.303§	4 (6.3)	2 (3.1)	0.680§
Diabetes mellitus	29 (35.4)	26 (26.0)	0.171	22 (34.4)	17 (26.6)	0.337
preoperative data						
Tumor side left	46 (56.1)	47 (47.0)	0.222	30 (46.9)	34 (53.1)	0.480
right	36 (43.9)	53 (53.0)		34 (53.1)	30 (46.9)	
Radiographic tumor size (cm)	7.5 (6.9–8.3)	8.5 (6.8–10.5)	0.006&	7.8 (7.0–8.6)	8.2 (7.0–10.0)	0.097&
Use of α adrenoreceptor blocker	56 (68.3)	40 (40.0)	< 0.001	38 (59.4)	39 (60.9)	0.857
Use of blood transfusion	23 (28.0)	28 (28.0)	0.994	19 (29.7)	21 (32.8)	0.703
24 h urine VMA/normal upper limit value	1.3 (0.5–2.2)	1.4 (0.4–2.5)	0.750&	1.3 (0.4–2.5)	1.3 (0.5–2.4)	0.899&

Continuous variables with normal distribution are reported as the mean ± standard deviation (SD); non-normal continuous variables are expressed as the median (interquartile range); categorical variables are reported as the number (percentage). Independent sample Student's t-test was used to compare the means of two continuous normally distributed variables and the Mann-Whitney *U* test was used to compare the means of two continuous non-normally distributed variables. The Chi-square test or Fisher' exact test was used for categorical variables. Recurrence and survival rates were calculated by Kaplan-Meier plots with the log-rank test. & Mann-Whitney *U* test, § Fisher' exact test, & Log-rank test. LA, laparoscopic adrenalectomy; OA open adrenalectomy; BMI, body mass index; ASA, American Society of Anesthesiologists, VMA, vanillylmandelic acid.

with OA were balanced into 64 pairs.

In the matched group, the mean age of the patients in the LA and OA groups was 51.9 and 51.7 years, respectively. Most patients were females (57.8% vs. 51.6%). The BMI was 23.4 and 23.1 kg/m², the majority of patients (79.7% and 82.8%) had low ASA scores (0–2), 57.8% and 67.2% of the patients had hypertension (continuous or intermittent), and the mean tumor size was 7.8 and 8.2 cm in the LA and OA groups, respectively.

The following three baseline variables were unbalanced between the LA and OA groups before PSM: proportion of patients with hypertension; use of an α -adrenoreceptor antagonist; and radiologic tumor size. A balance was obtained after adjusting these variables with PSM. The other pre-operative variables were not significantly different between the two groups, including BMI, comorbidity, blood transfusion, and 24-h urine VMA within the normal upper limit value before and after PSM (Table 1).

The incidence of IHD, blood transfusion rate during surgery, prolonged hypotension, and cardiovascular morbidity in the LA group were lower than the OA group (25% vs. 48.4%, 29.7% vs. 46.9%, 4.7% vs. 23.4%, and 14.1% vs. 37.5%, respectively). There was also less estimated blood loss and quicker bowel recovery in the LA group (100 ml vs. 300 ml and 1.9 d vs. 2.3 d) compared to the OA group. All of these differences were statistically significant.

The operative time (154 min vs. 150 min), length of hospital stay (9.8 d vs. 10.1 d), and post-operative blood transfusion rates (12.5% vs. 7.8%) were similar between the two groups. No patients died in the LA group and two patients (3.1%) died in the OA group, post-operatively. The proportion of patients in whom the blood pressure normalized was not significantly different (56.8% vs. 41.9%) between the two groups (Table 2). The recurrence rate (4.7% vs. 1.6%) and survival ($p = 0.763$) were also comparable (Table 2 and Fig. 3) with a median follow-up period of 36.0 and 65.0 months, respectively.

The surgical approach (OA vs. LA) was an independent risk factor for IHD, prolonged hypotension, and cardiovascular disease (CVD)

morbidity, as determined through multivariate binary logistic regression by adjusting variables; the ORs of OA compared to LA were 2.556 ($P = 0.025$), 4.293 ($P = 0.043$), and 3.055 ($P = 0.025$), respectively. The surgical approach also influenced bowel recovery ($\beta = 0.360$, $P < 0.001$), as determined by multiple linear regression analyses (Table 3).

4. Discussion

LA has become the standard treatment for almost all adrenal tumors since it was first used by Gagner in 1992 [11]. It is clear that LA is minimally invasive and is associated with less blood loss, quicker bowel recovery, and a shorter hospital stay compared with OA in small adrenal tumors [12]. With more experience and improvement in laparoscopic instruments, the indications for LA have expanded. Pheochromocytoma differ from other adrenal tumors because of uncontrolled catecholamine excretion, large tumor size, rich vascularity, and tight adherence to adjacent organs [13]. These factors make surgery involving pheochromocytoma more challenging. Indeed, studies focusing on whether or not LA is superior to OA for large pheochromocytoma are limited in number and no randomized control trials have been conducted. Thus, the current PSM cohort provides the fairest retrospective comparison.

After PSM, the baseline variables were balanced. The LA group had a lower incidence of IHD, transfusion requirements, prolonged hypotension post-operatively, and cardiovascular morbidity, less blood loss, and quicker bowel recovery compared with the OA group, while the operative time, rate of blood pressure normalization within 3 months, and recurrence and survival rates were comparable between the two groups. The surgical approach was an independent risk factor for IHD, prolonged hypotension, CVD morbidity, and longer bowel recovery.

IHD is the most important operative and anesthetic challenge during resection of a pheochromocytoma, and has been shown to be an independent risk factor for severe all-cause and cardiovascular-specific

Table 2
Peri-operative and prognostic data of patients undergoing pheochromocytoma adrenalectomy in this cohort.

Variable	Propensity before 182 patients			Propensity after 128 patients		
	LA	OA	P value	LA	OA	P value
Number of patients (%)	82 (100)	100 (100)		64 (100)	64 (100)	
Follow up period, months	38.0 (16.0–60.0)	73.0 (47.0–106.0)		36 (12.6–56.0)	65.0 (34.5–91.5)	
Intraoperative data						
IHD	22 (26.8)	43 (43.0)	0.023	16 (25.0)	31 (48.4)	0.006
Duration of operative time (minutes)	167.0 (120.0–222.0)	150.0 (106.0–205.0)	0.338&	154.0 (117.8–222.8)	150.0 (116.3–205.0)	0.810&
Estimated blood loss (ml)	100.0 (95.0–200.0)	400.0 (200.0–700.0)	< 0.001&	100.0 (85.0–200.0)	300.0 (200–675.0)	< 0.001&
Blood transfusion rate	21 (25.9)	49 (49.0)	0.001	19 (29.7)	30 (46.9)	0.045
Postoperative data						
Bowel recovery (days)	2.0 ± 0.4	2.3 ± 0.5	< 0.001	1.9 ± 0.5	2.3 ± 0.6	< 0.001
Duration of postoperative hospital stay	9.8 ± 4.3	10.0 ± 4.1	0.800	9.8 ± 4.4	10.1 ± 4.5	0.738
Prolonged hypotension after surgery	6 (7.3)	22 (22.0)	0.006	3 (4.7)	15 (23.4)	0.002
Blood transfusion rate after surgery	9 (11.0)	12 (12.0)	0.830	8 (12.5)	5 (7.8)	0.380
Severe morbidity (≥ Clavien II)	19 (23.2)	36 (36.0)	0.061	13 (20.3)	21 (32.8)	0.109
CVD morbidity	15 (18.3)	33 (33.0)	0.025	4 (14.1)	24 (37.5)	0.002
Perioperative mortality	0 (0.0)	2 (2.0)	0.502§	0 (0.0)	2 (3.1)	0.496§
Follow up data						
Rate of BP return to normal within 3 months	41 (50)	34 (34)	0.029	21 (56.8)	18 (41.9)	0.184
Recurrence and metastasis	3 (3.7)	2 (2.0)	0.308&	3 (4.7)	1 (1.6)	0.197&
Survive	2 (2.4)	7 (7.0)	0.575&	2 (3.1)	4 (6.2)	0.763&

Continuous variables with normal distribution are reported as the mean ± standard deviation (SD); non-normal continuous variables are expressed as the median (interquartile range); categorical variables are reported as the number (percentage). Independent sample Student's t-test was used to compare the means of two continuous normally distributed variables and the Mann-Whitney U test was used to compare the means of two continuous non-normally distributed variables, The Chi-square test or Fisher' exact test was used for categorical variables. Recurrence and survival rates were calculated by Kaplan-Meier plots with the log-rank test. & Mann-Whitney U test, § Fisher' exact test, & Log-rank test.

LA, laparoscopic adrenalectomy, OA open adrenalectomy, BMI, body mass index, ASA, American Society of Anesthesiologists, VMA, vanillylmandelic acid.

morbidity [13]. Previous reports have shown that IHD occurs in 39%–48% of pheochromocytoma resections [14,15]. In our study, the incidence of IHD was 25% and 48% in the LA and OA groups, respectively, with a statistically significant difference. The difference may be caused by less direct tumor manipulation and earlier ligation of the adrenal vein in the LA group compared with the OA group, which would lead to decreased secretion of catecholamines. The full exposure and magnified surgical vision in LA with the help of assistant trocar contributed to this finding. Kiernan et al. [16] reported that the incidence of IHD in OA was 27 times greater than LA. Other studies [17,18] have reported that circulating catecholamine levels are increased during the LA approach, but to a much lesser extent compared to the OA approach, which is consistent with our results. Indeed, the OA approach was confirmed to be an independent risk factor for IHD in the current study (OR = 2.556, P = 0.025).

The estimated blood loss was less (100 ml vs. 300 ml) and the transfusion rate was lower (29.7% vs. 46.7%) in the LA group compared

to the OA group. The magnified laparoscopic vision is superior to the open approach when manipulating small blood vessels and performing fine dissection [6]. Bin Lang et al. [19] reported similar findings between retroperitoneal LA and OA in a retrospective study.

There was no significant difference between the operative times for the two groups (154 min vs. 150 min, P = 0.810). Bin Lang et al. [19] reported that retroperitoneal LA required less operative time compared with OA (52 min vs. 120 min, P < 0.001) in a retrospective study, which was inconsistent with our study. The discrepancy may be because the tumors in our cohort were larger pheochromocytoma (≥ 6 cm), which likely involved more complex anatomy and required longer operative times.

The incidence of prolonged hypotension was lower in the LA group compared with the OA group (4.7% vs. 23.7%, P = 0.002). Hypotensive episodes often occur after resection of a pheochromocytoma [3] because of the dramatic decrease in catecholamine level, inadequate effective circulating blood volume, or residual α-adrenoreceptor

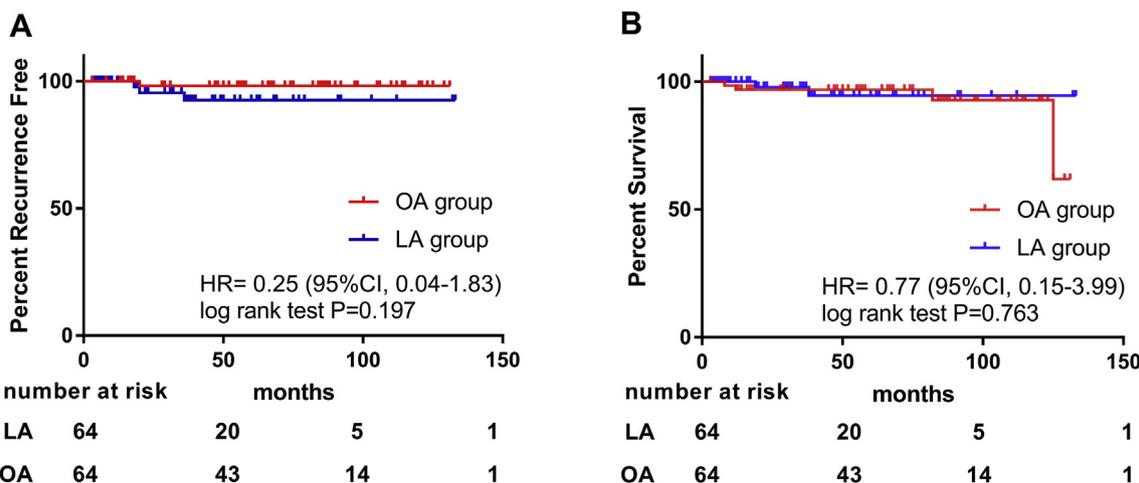


Fig. 3. Recurrence free rate and survival of the LA and OA groups, A recurrence free rate, B survival, LA, laparoscopic adrenalectomy; OA, open adrenalectomy.

Table 3
Regression analyses of patients surgical approach OA versus LA.

Variable	Propensity before (182 patients)			Propensity after (128 patients)		
	OR/ β	95% CI	P	OR/ β	95% CI	P
IHD&	1.677	0.826–3.408	0.153	2.556	1.128–5.795	0.025
Prolonged hypotension after surgery&	2.013	0.716–5.662	0.185	4.293	1.046–17.628	0.043
CVD morbidity&	1.392	0.640–3.027	0.404	3.055	1.148–8.1347	0.025
Blood transfusion rate during surgery&	1.994	1.010–3.938	0.047	1.635	0.750–3.566	0.216
Estimated blood loss§	169.125	27.625–310.626	0.019	157.890	–13.994–329.773	0.071
Bowel recovery§	0.353	0.191–0.516	< 0.001	0.360	0.169–0.558	< 0.001

The odds ratio and 95% confidence interval were determined by multivariate binary logistic regression and the β coefficient was calculated by multiple linear regression. & binary logistic regression, § multiple linear regression.

OR, odds ratio; CI, confidence interval; IHD, intra-operative hemodynamic instability; CHD, coronary heart disease.

medication level. Kiernan et al. [16] found that prolonged hypotension was significantly more frequent after OA in a univariate analysis, but the finding was not confirmed in a multivariate model when tumor size was included. In the current study, the open approach was confirmed to be an independent risk factor for prolonged hypotension based on multivariate regression (OR = 4.293, P = 0.043), which yielded a definitive conclusion regarding this issue.

We used the Clavien cLASification for evaluating complications of pheochromocytoma, and focused on cardiovascular morbidity, which was more closely related to pheochromocytoma surgery and treatment. The proportion of CVD morbidity in the LA group was lower than the OA group (14.1% vs. 34.5%, P = 0.002) and the open approach was an independent risk factor for CVD morbidity (OR = 3.055, P = 0.025). In agreement with these findings, Bin Lang et al. [19] also reported that there was less catecholamine release and a lower incidence of IHD in patients undergoing LA, thus resulting in less CVD morbidity. Two patients died during the peri-operative period due to CVD morbidity, both of whom underwent OA.

Patients who underwent LA had quicker bowel recovery than patients who underwent OA (1.9 d vs. 2.3 d), which was consistent with another report [20], and the open approach was an independent risk factor for bowel recovery in the current study (β = 0.360, P < 0.001).

The rate of blood pressure normalization within 3 months was 56.8% and 41.9% in the LA and OA groups, respectively; the difference was not statistically significant. After a long follow-up period, the recurrence (4.7% vs. 1.6%, P = 0.197) and survival (P = 0.763) were comparable between the LA and OA groups. The recurrence rate for patients with pheochromocytoma has not been established; however, 6.5%–16.5% of these patients will develop recurrences [21–23] in some studies were reported, which is slightly higher than our results.

One of the important issues involving the current study was that only patients with tumors size \leq 12 cm were included in the LA group after PSM, so all of the above conclusions were based on patients with tumors size between 6 and 12 cm in diameter.

At present, laparoscopic adrenalectomy has become the standard of care for surgical resection of the adrenal gland tumors. It can be divided into transperitoneal approach and retroperitoneal approach, Conzo G demonstrated in a review that retroperitoneal adrenalectomy is superior or at least comparable to transperitoneal adrenalectomy in many aspects, such as operation time, pain score, blood loss, hospitalization, complications rates and return to normal activity, even for tumors larger than 6 cm. But in this study, all laparoscopic adrenalectomy were undertaken by transperitoneal approach, so further studies are needed to evaluate the difference between these two kinds of techniques [24].

There were several limitations to this study. First, this was a retrospective study with selective data, even though PSM accounted for this effect. Second, there were various pre-operative management strategies and anesthesia protocols which were not standardized; these differences may have played a role in the final results. Third, the volume of patients were limited. Fourth, the follow-up period was not

equal between the two groups because we have used laparoscopy more frequently in recent years. A multi-center randomized controlled trial with standardization of pre-operative medical preparation and anesthesia management is warranted.

5. Conclusions

This propensity score-matched cohort study showed that LA was feasible, safe, and superior to OA for patients with large pheochromocytoma, meanwhile had comparable oncological outcomes after a lengthy follow-up.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Financial disclosures

Bin Wu certifies that all conflicts of interest, including specific financial interests, relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

(eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are none.

Disclosures

There is nothing to disclose.

Song Bai, Zichuan Yao, Xianqing Zhu, Zidong Li, Yunzhong Jiang, Rongzhi Wang, Bin Wu.

Ethical approval

Ethical approval (Ethics Committee No. 2018PS398K) was provided by the Institutional Research and Ethics Committee of the Shengjing Hospital Affiliated China Medical University in Shengyang, China. Informed consent was obtained from all eligible patients.

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Author contribution

Bin Wu had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Bin Wu.

Acquisition of data, analysis and interpretation of data: Song Bai, Zichuan Yao and Xianqing Zhu.

Drafting of the manuscript and critical revision of the manuscript for important intellectual content: Song Bai.

Statistical analysis: Rongzhi Wang, Zidong Li.

Obtaining funding and other (figures): Song Bai, Zidong Li, Yuzhong Jiang.

Conflicts of interest

None.

Research registration number

Chinese Clinical Trial Registry.

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Guarantor

Bin Wu.

Data Statement

We retrospectively studied 182 patients with radiographic tumor sizes ≥ 6 cm who underwent adrenalectomy at our center between 1 January 2007 and 31 December 2017. After propensity score-matching to balance baseline variables, 82 patients treated with LA and 100 patients treated with OA were grouped into 64 pairs. Patient demographics, and extensive peri-operative and oncologic data were recorded and compared. An independent sample Student's *t*-test was used to compare the means of two continuous normally distributed variables and the Mann-Whitney U test was applied to compare the means of two continuous non-normally distributed variables. Pearson's chi-square test or Fisher's exact test was used for categorical variables. Recurrence and survival rates were calculated using Kaplan-Meier curves with a log-rank test. The adjusted odds ratio (OR) and 95% confidence interval (CI) were determined by binary logistic regression and the β coefficient was calculated by multiple linear regression. Values of $P < 0.05$ (two-tailed) were considered statistically significant. In the matched group, the incidence of intra-operative hemodynamic instability, transfusion rate, prolonged hypotension, and cardiovascular morbidity in the LA group were lower than the OA group (25.0% vs. 48.4%, 29.7% vs. 46.9%, 4.7% vs. 23.4%, and 14.1% vs. 37.5%, respectively). The estimated blood loss was less (100 ml vs. 300 ml) and bowel recovery was quicker (1.9 d vs. 2.3 d) in the LA group. The proportion of patients in whom blood pressure returned to normal ($P=0.184$), had recurrences ($P=0.197$), and survived ($P=0.763$) were equivalent. The surgical approach (OA vs. LA) was an independent risk factor for IHD, prolonged hypotension, cardiovascular morbidity, and longer bowel recovery.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijssu.2018.11.018>.

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