

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

ScienceDirect

journal homepage: [www.elsevier.com/locate/ajur](http://www.elsevier.com/locate/ajur)

Original Article

# Surgical treatment of large pheochromocytoma (> 6 cm): A 10-year single-center experience

Liang Zhang <sup>a,1</sup>, Danlei Chen <sup>a,1</sup>, Yingxian Pang <sup>a</sup>, Xiao Guan <sup>a,b</sup>, Xiaowen Xu <sup>a</sup>, Cikui Wang <sup>a</sup>, Qiao Xiao <sup>a</sup>, Longfei Liu <sup>a,b,\*</sup>

<sup>a</sup> Department of Urology, Xiangya Hospital, Central South University, Changsha, China

<sup>b</sup> National Clinical Research Center for Geriatric Disorders, Xiangya Hospital, Central South University, Changsha, China

Received 21 July 2021; received in revised form 20 March 2022; accepted 15 April 2022

Available online 20 June 2022



## KEYWORDS

Pheochromocytoma;  
Laparoscopic  
adrenalectomy;  
Open adrenalectomy;  
Surgery;  
Treatment

**Abstract** *Objective:* Clinical practice guidelines recommend open adrenalectomy (OA) for large pheochromocytoma (LPCC) > 6 cm in size. Although laparoscopic adrenalectomy (LA) for the treatment of LPCC has been reported, its role remains unclear. This study aimed to compare the effectiveness of LA and OA, and summary the surgical treatment experience.

*Methods:* Data concerning LPCC, from January 2010 to June 2019 of a single institution, were retrospectively reviewed. Altogether 82 patients with a tumor larger than 6 cm were included (52 patients in LA group and 30 patients in OA group). Groups were balanced by propensity score matching (PSM) into 15 pairs. Patients' demographics, preoperative characteristics, and prognosis were analyzed.

*Results:* Before PSM, the OA group had larger tumor sizes (median [interquartile range, IQR]: 8.9 [7.3–10.3] vs. 7.2 [6.7–8.0] cm;  $p=0.000$ ) and higher vanillylmandelic acid level (median [IQR]: 114.3 [67.8–326.4] vs. 66.6 [37.8–145.8]  $\mu\text{mol}/24\text{ h}$ ;  $p=0.004$ ) and needed a higher cumulative dose of prazosin (median [IQR]: 83.5 [37.0–154.0] vs. 38.0 [21.0–81.0] mg;  $p=0.028$ ). After PSM, the baseline data showed no significant differences between both groups. The LA group had relatively more stable blood pressure in surgery, with a lower fluctuation of systolic blood pressure (mean  $\pm$  standard deviation [SD]: 70.9  $\pm$  25.1 vs. 107.4  $\pm$  46.2 mmHg,  $p=0.012$ ) and a lower percentage of hemodynamic instability (46.7% vs. 86.7%,  $p=0.020$ ). The LA group had shorter postoperative hospital stays (mean  $\pm$  SD: 6.4  $\pm$  2.7 vs. 10.1  $\pm$  3.4 days;  $p=0.003$ ) than the OA group. Differences regarding metastasis rate (6.7% vs. 0,  $p=1.000$ ) were not statistically significant between LA and OA groups. The median

\* Corresponding author. Department of Urology, Xiangya Hospital, Central South University, Changsha, China.

E-mail address: [longfei\\_liu@csu.edu.cn](mailto:longfei_liu@csu.edu.cn) (L. Liu).

Peer review under responsibility of Tongji University.

<sup>1</sup> These authors contributed equally to the article.

(IQR) follow-up time of 82 patients was 72.5 (47.0–103.5) months. Binary logistic regression showed that right-side tumors or those >8 cm in size were independent risk factors of OA. **Conclusion:** LA is a safe, minimally invasive procedure for LPCC and has relatively better perioperative characteristics in large medical centers. Patients with tumors on the right side or larger than 8 cm are more likely to undergo OA initially.

© 2022 Editorial Office of Asian Journal of Urology. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

Pheochromocytomas (PCCs) and paragangliomas (PGLs), collectively termed as PPGLs, are neuroendocrine tumors that arise from the chromaffin cells of the adrenal medulla or extra-adrenal gland [1–3]. PPGLs can secrete catecholamines, which may lead to secondary hypertension. It has been reported that preoperative use of alpha-blockers is necessary for blood pressure control and surgical risk [4]. The alpha-adrenergic blockade is currently the first choice of preoperative treatment in patients with functional PCC and sympathetic PGL [5]. Giant PCC can lead to death from heart failure, so more rigorous surgical procedures are needed for giant PCC [6].

Approximately 10% of patients with PPGLs experience hypertensive crisis that causes dysfunction of multiple organs, such as the heart, lung, brain, and kidney, which may ultimately be life-threatening [1]. Surgical resection is the standard treatment for PPGLs [7].

Laparoscopic adrenalectomy (LA) has been proven to be an effective procedure for most PCCs and is widely used [8]. Although LA is reported to have positive therapeutic effects on small PCC ( $\leq 6$  cm), its use in the treatment of large pheochromocytoma (LPCC) remains controversial [8,9]. According to the guideline and consensus of PCC and PGL, LA should be performed for most PCCs, and open adrenalectomy (OA) should be performed for tumors larger than 6 cm or for invasive PGL to ensure complete tumor resection [10,11]. However, several studies suggested that LA is a safe and feasible procedure for large tumors [3,12–17]. The main limitations of previous studies include the limited number of cases and lack of long-term outcome comparison. Therefore, this study aimed to determine the effectiveness of LA versus OA and summarize our experience in treating LPCC.

## 2. Patients and methods

### 2.1. Patients

Between January 2010 and June 2019, 369 cases of pathologically confirmed PPGLs were treated at Xiangya Hospital, Changsha, China. Overall, 82 patients were finally included in this study after excluding bilateral PCC, small PCC, and PGL (Fig. 1). Eighty-two patients were divided into LA group ( $n=52$ ) and OA group ( $n=30$ ). We excluded the data from two patients who initially underwent LA and then converted to OA to not interfere with the perioperative characteristics of both groups. Both groups were compared for the

differences in postoperative outcomes and prognosis. The risk factors involving surgery decisions (LA or OA) were analyzed using binary logistic regression. This study was approved by the Ethics Committee of Xiangya Hospital of Central South University (No. 201905133), and informed consents were obtained from all patients.

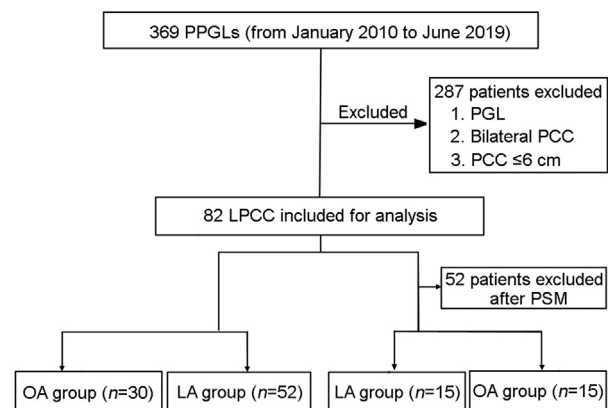
### 2.2. Operation technique

#### 2.2.1. Transperitoneal LA

The patient was in the supine position, and an appropriate operation hole was established according to the tumor position. First, we mobilized the right lobe of the liver for tumors on the right side; for left tumors we needed to mobilize the spleen and the tail of the pancreas. Then we freed along with the adrenal gland and around the tumor, separated and clamped the middle adrenal vein, and completely removed the tumor.

#### 2.2.2. Retroperitoneal LA

The patient was in the lateral position. Surgeons used a balloon to dilate the retroperitoneal space and established an appropriate operation hole. First, we incised the perirenal fascia with an ultrasonic scalpel, freed the upper pole of the kidney close to the surface of the renal capsule, and found the adrenal gland at the peritoneal fold above the inner side of the upper pole of the kidney. When removing the tumor on the right side, the central adrenal vein was



**Figure 1** Flow chart of the study. PCC, pheochromocytoma; LPCC, large PCC; PGL, paraganglioma; PPGLs, PCCs and PGLs; LA, laparoscopic adrenalectomy; OA, open adrenalectomy; PSM, propensity score matching.

separated upward along the outer edge of the inferior vena cava; for tumor on the left side, the central adrenal vein was searched above the renal pedicle. When the central adrenal vein was fully exposed, we double ligated the vessel with vascular clips and severed it. After dissection of the adrenal gland along the adrenal capsule surface, the tumor was completely resected.

### 2.2.3. OA

The patient was in the supine position, and the appropriate incision was selected. For the right tumor, the right lobe of the liver should be pushed aside, while for the left tumor, the interference of the spleen and the tail of the pancreas should be avoided. The tissue around the tumor was carefully dissected. Then the central adrenal vein was exposed, double ligated. Finally, we removed the tumor completely.

## 2.3. Data collection

The patients' demographic data and perioperative characteristics were collected through electronic medical records, and prognostic data were obtained through outpatient review and regular follow-up. Age, sex, clinical manifestations, preoperative blood pressure, heart rate (HR), vanillylmandelic acid (VMA) level, prazosin consumption, tumor size, tumor location, operating time, blood loss, hemodynamics, postoperative recovery, recurrence, and metastasis were collected.

Alpha-receptor blocker (mainly prazosin in our center) and beta-receptor blocker (if needed) were administered to achieve ideal blood pressure (approximately 120/80 mmHg) and HR (about 80 beats per minute) control. Preoperative systolic blood pressure (SBP) and diastolic blood pressure (DBP) referred to the maximum value preoperatively. Hemodynamic instability (HI) was defined as an intraoperative SBP of  $>180$  mmHg or a mean arterial pressure of  $<60$  mmHg. The fluctuation in SBP (distance between maximum and minimum values) during the operation was also recorded.

The maximum on imaging determines tumor size. All patients underwent radial artery puncture and electrocardiogram monitoring before surgery. An anesthesiologist measured blood pressure through continuous intra-arterial measurements during surgery. Blood pressure and HR were recorded every 5 min based on real-time monitoring data. Anesthesia monitor plotted the trends in blood pressure and HR, allowing us to capture extreme values of SBP, DBP, and HR during surgery.

## 2.4. Propensity score matching (PSM)

We used the PSM method to adjust the baseline differences between groups to draw more reliable conclusion. Multivariate logistic regression was used to determine propensity scores for each patient based on age, preoperative blood pressure, VMA level, use of the alpha-adrenoceptor blocking drug, tumor size, and tumor laterality. LA and OA groups were matched 1:1 using a caliper

width of 0.1 for the propensity score through nearest neighbor matching (Fig. 1).

## 2.5. Statistical analysis

All analyses were performed using SPSS version 22.0 (SPSS, Chicago, IL, USA). Continuous variables were expressed as mean $\pm$ SD, and categorical variables were presented as numbers and percentages for descriptive statistics. Data with non-normal distributions were presented as medians and interquartile ranges (IQR). The two groups were compared using an independent *t*-test, Chi-square, and Fisher's exact tests for normally distributed data, and the Mann-Whitney *U* test was used for non-normally distributed data. Binary logistic regression analysis determined the odds ratio (OR) and 95% confidence interval (CI). A two-sided *p*-value of  $<0.05$  was considered statistically significant.

## 3. Results

### 3.1. Baseline data of the LA and OA groups

The study included 82 patients with LPCC who were divided into the LA ( $n=52$ ) and OA ( $n=30$ ) groups. No significant differences were found between the LA and OA groups regarding age or sex. The preoperative SBP (median [IQR]: 176 [140–200] vs. 155 [140–197] mmHg;  $p=0.187$ ), DBP (median [IQR]: 98 [84–110] vs. 90 [80–102] mmHg;  $p=0.119$ ), or HR (mean $\pm$ SD: 96.1 $\pm$ 16.1 vs. 94.7 $\pm$ 11.1 beats per minute;  $p=0.684$ ) between the LA and the OA group showed no significant differences.

Before PSM, the OA group had larger tumor sizes (median [IQR]: 8.9 [7.3–10.3] vs. 7.2 [6.7–8.0] cm;  $p=0.000$ ) and higher VMA level (median [IQR]: 114.3 [67.8–326.4] vs. 66.6 [37.8–145.8]  $\mu\text{mol}/24$  h;  $p=0.004$ ) and needed a higher cumulative dose of prazosin (median [IQR]: 83.5 [37.0–154.0] vs. 38.0 [21.0–81.0] mg;  $p=0.028$ ).

After PSM, 82 patients were paired into 30 patients and the differences in baseline characteristics were balanced (Table 1). The median (IQR) VMA level between LA and OA groups showed no significant difference (92.9 [37.8–170.8]  $\mu\text{mol}/24$  h vs. 104.6 [67.8–326.4]  $\mu\text{mol}/24$  h,  $p=0.237$ ). There was no significant difference in the cumulative dose of prazosin between LA and OA groups (median [IQR]: 47.0 [16.5–108.0] vs. 60.0 [37.0–154.0] mg,  $p=0.300$ ). In addition, the median (IQR) tumor sizes were 8.0 (7.0–8.0) cm and 8.9 (7.3–10.3) cm in the LA and OA groups, respectively ( $p=0.228$ ).

### 3.2. Perioperative characteristics and prognoses of both groups

The LA group showed no advantage in operating time before or after PSM. Before PSM, those patients that underwent OA had larger estimated blood loss (median [IQR]: 750 [375–2125] vs. 350 [150–1000] mL,  $p=0.003$ ). Besides,

**Table 1** Baseline characteristics of patients with LPCC underwent LA or OA.

Variable	Before PSM			After PSM		
	LA (n=52)	OA (n=30)	p-Value	LA (n=15)	OA (n=15)	p-Value
Age <sup>a</sup> , year	49.5±13.3	47.8±9.9	0.504	51.8±13.6	47.3±7.9	0.288
Female, n (%)	27 (51.9)	12 (40.0)	0.298	6 (40.0)	5 (33.3)	0.705
Preoperative SBP <sup>b</sup> , mmHg	176 (140–200)	155 (140–197)	0.187	150 (131–185)	157 (140–197)	0.803
Preoperative DBP <sup>b</sup> , mmHg	98 (84–110)	90 (80–102)	0.119	91 (82–100)	92 (80–102)	0.819
Preoperative HR <sup>a</sup> , beats per min	96.1±16.1	94.7±11.1	0.684	98.3±12.4	96.2±13.4	0.664
VMA <sup>b</sup> , μmol/24 h	66.6 (37.8–145.8)	114.3 (67.8–326.4)	0.004	92.9 (37.8–170.8)	104.6 (67.8–326.4)	0.237
Cumulative dose of prazosin <sup>b</sup> , mg	38.0 (21.0–81.0)	83.5 (37.0–154.0)	0.028	47.0 (16.5–108.0)	60.0 (37.0–154.0)	0.300
Tumor size <sup>b</sup> , cm	7.2 (6.7–8.0)	8.9 (7.3–10.3)	0.000	8.0 (7.0–8.0)	8.9 (7.3–10.3)	0.228
Laterality (left, n [%])	27 (51.9)	12 (40.0)	0.298	6 (40.0)	6 (40.0)	1.000

LPCC, large pheochromocytoma; LA, laparoscopic adrenalectomy; OA, open adrenalectomy; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; VMA, vanillylmandelic acid; PSM, propensity score matching.

<sup>a</sup> Values are presented as mean±standard deviation.

<sup>b</sup> Values are presented as median (interquartile range).

a higher proportion of patients in OA group required transfusion (76.7% vs. 46.0%,  $p=0.007$ ). However, no significant differences were found regarding blood loss and transfusion after adjusting the baseline data. After PSM, LA group was still better than OA group in intraoperative blood pressure and postoperative recovery. The LA group had relatively more stable blood pressure in surgery, with a lower fluctuation of SBP (mean±SD: 70.9±25.1 vs. 107.4±46.2 mmHg,  $p=0.012$ ) and a lower percentage of HI (46.7% vs. 86.7%,  $p=0.020$ ). A smaller proportion of patients in the LA group were required to transfer to the intensive care unit (20.0% vs. 53.3%;  $p=0.058$ ) even though no significant difference was found. Furthermore, the LA group had shorter postoperative hospital stays (mean±SD: 6.4±2.7 vs. 10.1±3.4 days,  $p=0.003$ ). The results of long-term follow-up were also shown in Table 2. The median (IQR) follow-up time of 82 patients was 72.5 (47.0–103.5)

months, and no significant difference in follow-up time between groups was found. We found that differences regarding metastasis rate (6.7% vs. 0,  $p=1.000$ ) were not statistically significant.

### 3.3. Risk factors involving decision-making on surgery

To explore the factors that may affect surgeons' decision-making process, we performed binary logistic regression analysis on all 82 patients. Binary logistic regression analysis was performed based on univariate analysis, considering age, sex, VMA level, tumor size, and laterality. Notably, tumors on the right side (OR, 5.192; 95% CI, 1.121–24.044;  $p=0.035$ ) and with the size range of >8 cm (OR, 18.087; 95% CI, 1.499–218.148;  $p=0.023$ ) were independent risk factors of OA (Table 3).

**Table 2** Perioperative and follow-up outcomes of LPCC patients.

Variable	Before PSM			After PSM		
	LA <sup>c</sup> (n=50)	OA (n=30)	p-Value	LA (n=15)	OA (n=15)	p-Value
Operating time <sup>a</sup> , min	155 (130–206)	153 (109–224)	0.578	150 (124–291)	185 (103–248)	0.819
EBL <sup>a</sup> , mL	350 (150–1000)	750 (375–2125)	0.003	425 (175–1938)	1500 (450–2600)	0.136
Transfusion, n (%)	23 (46.0)	23 (76.7)	0.007	11 (73.3)	13 (86.7)	0.651
Fluctuation of SBP <sup>b</sup> , mmHg	65.4±30.5	94.4±41.4	0.001	70.9±25.1	107.4±46.2	0.012
HI, n (%)	19 (38.0)	19 (63.0)	0.028	7 (46.7)	13 (86.7)	0.020
ICU stay, n (%)	8 (16.0)	13 (43.3)	0.007	3 (20.0)	8 (53.3)	0.058
Postoperative hospital stay <sup>b</sup> , day	6.5±3.2	8.7±3.4	0.002	6.4±2.7	10.1±3.4	0.003
Conversion <sup>c</sup> , n (%)	2/52 (3.8)	0	—	—	—	—
Recurrence, n (%)	4 (8.0)	0	0.291	0	0	—
Metastasis, n (%)	2 (4.0)	1 (3.3)	1.000	1 (6.7)	0	1.000
Follow-up period <sup>a</sup> , month	77.5 (49.8–109.0)	62.5 (46.5–79.0)	0.082	81.0 (49.0–113.0)	74.0 (47.0–89.0)	0.229

LPCC, large pheochromocytoma; OA, open adrenalectomy; LA, laparoscopic adrenalectomy; EBL, estimated blood loss; HI, hemodynamic instability; ICU, intensive care unit; SBP, systolic blood pressure; PSM, propensity score matching; —, not available.

<sup>a</sup> Values are presented as median (interquartile range).

<sup>b</sup> Values are presented as mean±standard deviation.

<sup>c</sup> Two patients converted to OA, and their perioperative data were not included in the analysis.

**Table 3** Binary logistic regression of the surgical approach: OA versus LA.

Variable	B	OR	95% CI	<i>p</i> -Value <sup>a</sup>
Age	-0.018	0.982	0.930–1.037	0.518
Sex (male)	0.744	2.105	0.494–8.970	0.314
VMA	0.004	1.004	0.997–1.011	0.223
Tumor size				
>7 cm	0.018	1.018	0.216–4.812	0.982
>8 cm	2.895	18.087	1.499–218.148	0.023
>9 cm	-0.550	0.577	0.051–6.468	0.656
Tumor laterality (right)	1.647	5.192	1.121–24.044	0.035

OA, open adrenalectomy; LA, laparoscopic adrenalectomy; B, regression coefficient; OR, odds ratio; CI, confidence interval; VMA, vanillylmandelic acid.

<sup>a</sup> The LA group was used as the control group.

#### 4. Discussion

LA for treating small PCC has been deemed a safe and minimally invasive procedure; however, only a limited number of studies have compared the differences in efficacy between LA and OA for LPCC [17–19]. Although LA has been successfully used for the treatment of LPCC, the effectiveness of LA for the treatment of LPCC has not been well defined [20,21], and the current guidelines recommended OA, rather than LA, for the treatment of tumors larger than 6 cm [10,11]. However, our results showed that LA can be safely conducted and had better perioperative outcomes for LPCC patients when compared with OA. Moreover, patients with tumors on the right side or those larger than 8 cm in size appear more likely to undergo OA.

This study has reviewed 10-year experience in treating LPCCs, which were larger than 6 cm, analyzing the baseline characteristics, perioperative outcomes, and long-term follow-up results. We also used the PSM method to balance the baseline differences caused by non-randomization to draw more reliable conclusions. After PSM, our series showed that LPCC can be removed safely, and patients got benefit from LA.

Of 82 LPCC cases, 52 were planned to undergo LA, and 50 (96.2%) were completed. Only two cases initially planned for LA were converted to OA; one had sharply increased blood pressure which fluctuated up to 228 mmHg, and another was transformed to OA because of large tumor size (10 cm). Besides, the LA group has more advantages in some perioperative indicators, such as less HI, minor fluctuation of SBP, and faster recovery from the hospital, which have been described in a previous study [22].

HI has always been a major concern during the resection of PCC; the reported incidences of HI during PCC resection ranged from 17% to 83% [22,23], which was consistent with the findings of our study. Patients in the LA group showed more stable hemodynamics than those in the OA group, with a lower rate of HI than those in the OA group (46.7% vs. 86.7%,  $p=0.020$ ). The magnified visions and high-energy hemostatic devices in LA allowed surgeons to reduce direct manipulation of the tumor and also be able to ligate the central adrenal vein early, which would minimize

catecholamine secretion. However, for LPCC, LA imposes more pressure on surgeons because the operation space under endoscopy is smaller, which may require a longer operation time and even higher blood loss than expected. Indeed, in this study, the LA group was not better than OA in estimated blood loss and operating time.

There were no significant differences in postoperative metastasis rates (6.7% vs. 0,  $p=1.000$ ) between the two groups, which is consistent with the reports of previous studies [20,21]. As described by Bai et al. [21], the recurrence and metastasis rates between LA and OA were 4.6% and 1.6%, respectively, with a  $p$ -value of 0.197. Another research conducted by Wang et al. [20] showed a similar recurrence rate between LA and OA, 8.7% vs. 7.1%, respectively. It is worth noting that the prognosis of LA was comparable to that of OA according to the findings of this study and previous studies. Some researchers suggested that large tumor size is a predictor of malignancy; however, substantial evidence is lacking [24,25]. Considering its advantages, as previously described, we believe that LA can be used for LPCC if there is no preoperative metastasis and complete tumor resection can be achieved.

Even though the efficacy of LA in the treatment of LPCC is definite, it remains unclear when to choose LA or OA. Herein, we conducted binary logistic regression analysis and were delighted to find that OA was prone to be selected for treating larger LPCC (>8 cm) or tumors on the right side.

It was reported that LA is more difficult on the right side than on the left [26]. Anatomical factors, such as the right adrenal vein being shorter than the left and draining into the inferior vena cava, are often used to explain such differences [26–28]. To explore the challenging risk factors for right and left LA, Gunseren et al. [26] compared a total of 272 patient's medical records that underwent single side LA. In this study, 22 right-sided and 19 left-sided LA were performed in 41 PCC patients. No significant differences were found in perioperative parameters between the left and right LA groups. The study showed that right LA could be more dangerous than left-side LA in difficult adrenalectomy cases because cases with bleeding requiring erythrocyte replacement and the one case that was converted to open surgery were on the right side [26]. Chung et al. [29] reported that hypertension occurred more commonly during right adrenalectomy. Even though some studies [26,28] have demonstrated that perioperative factors like operating time and estimated blood loss showed similar results between both procedures, HI and bleeding often lead to conversion and are crucial factors for choosing OA, which may explain the tendency to conduct OA for tumors in the right side.

In our center, 63.4% of patients with LPCC were initially operated by LA, while 36.6% underwent OA; the results turned out that OA was still necessary for larger tumors. Papers published previously reported that tumor size was an independent risk factor for HI, conversion, and even malignancy—the larger the tumor diameter, the higher the risk [7,24,25,30]. We reported a series of LPCC patients on which surgeons challenged the guidelines (OA was recommended for larger than 6 cm PCC) and accumulated successful experience in treating LPCC, and these demonstrated that 6 cm might not be the most suitable index. As a large medical center, which has more than 800

adrenal tumor patients per year, the surgeons would prefer to challenge LA even for LPCC, which may lead to selection bias according to their experience. The binary logistic regression analysis showed that most LPCC could be conducted with LA in our center, while surgeons preferred to perform OA on tumors larger than 8 cm or on the right side.

This study had a few limitations. First, it was a non-randomized, retrospective, single-center study, with an unavoidable bias inherent in this study's design. Second, catecholamines in the blood and urine were not routinely measured, limiting analysis of biochemical phenotypes. Despite these limitations, our study fully demonstrated the effectiveness of LA for LPCC. More risk factors, such as tumor size and tumor laterality, should be considered to select a more appropriate surgical procedure. More importantly, starting a prospective, randomized study in the next stage is vital.

## 5. Conclusion

This study confirmed that LA is safe and minimally invasive in the treatment of LPCC, which showed relatively better perioperative characteristics and had similar oncological outcomes compared with OA. In addition, OA is still significant for the treatment of LPCC. Patients with tumors larger than 8 cm or located on the right side are more likely to receive OA.

## Author contributions

*Study concept and design:* Liang Zhang, Longfei Liu.

*Data acquisition:* Liang Zhang, Yingxian Pang, Xiao Guan, Xiaowen Xu, Cikui Wang, Qiao Xiao.

*Data analysis:* Liang Zhang, Danlei Chen.

*Drafting of manuscript:* Liang Zhang, Danlei Chen.

*Critical revision of the manuscript:* Liang Zhang, Danlei Chen, Longfei Liu.

## Conflicts of interest

The authors declare no conflict of interest.

## References

- [1] Nozaki T, Iida H, Morii A, Fujiuchi Y, Okumura A, Fuse H. Laparoscopic resection of adrenal and extra-adrenal pheochromocytoma. *J Endourol* 2013;27:862–8.
- [2] Neumann HPH, Young Jr WF, Eng C. Pheochromocytoma and Paraganglioma. *N Engl J Med* 2019;381:552–65.
- [3] Li M, Wang C, Liu P, Qi L, Chen X, Fan B, et al. Clinical and genetic features of pediatric PCCs/PGLs patients: a single-center experience in China. *Transl Androl Urol* 2020;9:267–75.
- [4] Castinetti F, De Fremerville JB, Guerin C, Cornu E, Sarlon G, Amar L. Controversies about the systematic preoperative pharmacological treatment before pheochromocytoma or paraganglioma surgery. *Eur J Endocrinol* 2022;186:D17–24. <https://doi.org/10.1530/EJE-21-0692>.
- [5] Zawadzka K, Wieckowski K, Malczak P, Wysocki M, Major P, Pedziwiatr M, et al. Selective vs. non-selective alpha-blockade prior to adrenalectomy for pheochromocytoma: systematic review and meta-analysis. *Eur J Endocrinol* 2021;184:751–60.
- [6] Nguyen DN, Qureshi JM, Singh H, Tran CD, Cothron K. Large malignant pheochromocytoma causing cardiac failure and metastasis: a case report with review of literature. *Curr Probl Diagn Radiol* 2021;50:961–6.
- [7] Ma L, Shen L, Zhang X, Huang Y. Predictors of hemodynamic instability in patients with pheochromocytoma and paraganglioma. *J Surg Oncol* 2020;122:803–8.
- [8] Zhu W, Wang S, Du G, Liu H, Lu J, Yang W. Comparison of retroperitoneal laparoscopic versus open adrenalectomy for large pheochromocytoma: a single-center retrospective study. *World J Surg Oncol* 2019;17:111. <https://doi.org/10.1186/s12957-019-1649-x>.
- [9] Shiraishi K, Kitahara S, Ito H, Oba K, Ohmi C, Matsuyama H. Transperitoneal versus retroperitoneal laparoscopic adrenalectomy for large pheochromocytoma: comparative outcomes. *Int J Urol* 2019;26:212–6.
- [10] Calissendorff J, Juhlin CC, Bancos I, Falhammar H. Pheochromocytomas and abdominal paragangliomas: a practical guidance. *Cancers* 2022;14:917. <https://doi.org/10.3390/cancers14040917>.
- [11] Lenders JW, Duh QY, Eisenhofer G, Gimenez-Roqueplo AP, Grebe SK, Murad MH, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2014;99:1915–42.
- [12] Dimas S, Roukounakis N, Kafetzis I, Bethanis S, Anthi S, Michas S, et al. Feasibility of laparoscopic adrenalectomy for large pheochromocytomas. *J Soc Laparoendosc Surg* 2007;11:30–3.
- [13] Indupur RR, Nerli RB, Reddy MN, Siddappa SN, Thakkar R. Laparoscopic adrenalectomy for large pheochromocytoma. *BJU Int* 2007;100:1126–9.
- [14] Ippolito G, Palazzo FF, Sebag F, Thakur A, Cherenko M, Henry JF. Safety of laparoscopic adrenalectomy in patients with large pheochromocytomas: a single institution review. *World J Surg* 2008;32:840–4; discussion 5–6.
- [15] Perry KA, El Youssef R, Pham TH, Sheppard BC. Laparoscopic adrenalectomy for large unilateral pheochromocytoma: experience in a large academic medical center. *Surg Endosc* 2010;24:1462–7.
- [16] Agarwal G, Sadacharan D, Aggarwal V, Chand G, Mishra A, Agarwal A, et al. Surgical management of organ-contained unilateral pheochromocytoma: comparative outcomes of laparoscopic and conventional open surgical procedures in a large single-institution series. *Langenbecks Arch Surg* 2012;397:1109–16.
- [17] Conzo G, Musella M, Corcione F, De Palma M, Avenia N, Milone M, et al. Laparoscopic treatment of pheochromocytomas smaller or larger than 6 cm. A clinical retrospective study on 44 patients. Laparoscopic adrenalectomy for pheochromocytoma. *Ann Ital Chir* 2013;84:417–22.
- [18] Aggeli C, Nixon AM, Parianos C, Vletsis G, Papanastasiou L, Markou A, et al. Surgery for pheochromocytoma: a 20-year experience of a single institution. *Hormones (Basel)* 2017;16:388–95.
- [19] Conzo G, Gambardella C, Candela G, Sanguinetti A, Polistena A, Clarizia G, et al. Single center experience with laparoscopic adrenalectomy on a large clinical series. *BMC Surg* 2018;18:2. <https://doi.org/10.1186/s12893-017-0333-8>.
- [20] Wang W, Li P, Wang Y, Wang Y, Ma Z, Wang G, et al. Effectiveness and safety of laparoscopic adrenalectomy of large pheochromocytoma: a prospective, nonrandomized, controlled study. *Am J Surg* 2015;210:230–5.
- [21] Bai S, Yao Z, Zhu X, Li Z, Jiang Y, Wang R, et al. Comparison of transperitoneal laparoscopic versus open adrenalectomy for large pheochromocytoma: a retrospective propensity score-matched cohort study. *Int J Surg* 2019;61:26–32.
- [22] Li J, Wang Y, Chang X, Han Z. Laparoscopic adrenalectomy (LA) vs. open adrenalectomy (OA) for pheochromocytoma

- (PHEO): a systematic review and meta-analysis. *Eur J Surg Oncol* 2020;46:991–8.
- [23] Scholten A, Vriens MR, Cromheecke GJ, Borel Rinkes IH, Valk GD. Hemodynamic instability during resection of pheochromocytoma in MEN versus non-MEN patients. *Eur J Endocrinol* 2011;165:91–6.
- [24] Korevaar TI, Grossman AB. Pheochromocytomas and paragangliomas: assessment of malignant potential. *Endocrine* 2011;40:354–65.
- [25] Wang Y, Li M, Deng H, Pang Y, Liu L, Guan X. The systems of metastatic potential prediction in pheochromocytoma and paraganglioma. *Am J Cancer Res* 2020;10:769–80.
- [26] Gunseren KO, Cicek MC, Vuruskan H, Kordan Y, Yavascaoglu I. Challenging risk factors for right and left laparoscopic adrenalectomy: a single centre experience with 272 cases. *Int Braz J Urol* 2019;45:747–53.
- [27] Rieder JM, Nisbet AA, Wuerstle MC, Tran VQ, Kwon EO, Chien GW. Differences in left and right laparoscopic adrenalectomy. *J Soc Laparoendosc Surg* 2010;14:369–73.
- [28] Kokorak L, Soltés M, Vladovic P, Marko L. Laparoscopic left and right adrenalectomy from an anterior approach—is there any difference? Outcomes in 176 consecutive patients. *Wideochir Inne Tech Maloinwazyjne* 2016;11:268–73.
- [29] Chung HS, Kim MS, Yu HS, Hwang EC, Kim SO, Oh KJ, et al. Laparoscopic adrenalectomy using the lateral retroperitoneal approach: is it a safe and feasible treatment option for pheochromocytomas larger than 6 cm? *Int J Urol* 2018;25:414–9.
- [30] Vidal O, Saavedra-Perez D, Martos JM, de la Quintana A, Rodriguez JI, Villar J, et al. Risk factors for open conversion of lateral transperitoneal laparoscopic adrenalectomy: retrospective cohort study of the Spanish Adrenal Surgery Group (SASG). *Surg Endosc* 2020;34:3690–5.