

Safety and feasibility of laparoscopic adrenalectomy for pheochromocytoma irrespective of tumor size

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Objective: Although laparoscopic adrenalectomy (LA) is recognized as the best modality for removing benign lesions of the adrenal gland, doubts about the use of LA for pheochromocytoma (PCC) remain. We evaluated the efficacy of LA for PCC on the basis of perioperative outcomes.

Methods: Twenty-three patients who underwent LA for PCC from April 1999 through November 2013 were included in the study. Five patients (21.7%) had a tumor size of ≥ 60 mm (large PCC cohort, LgPCC), and 18 (78.3%) had a tumor size of < 60 mm (small PCC cohort, SmPCC). Data were retrospectively reviewed from a prospectively maintained database at our institution.

Results: The median size of adrenal masses was 41 mm. Median estimated blood loss and operative time across all cases were 30 ml and 170 minutes, respectively. LA was completed successfully for 22 of the 23 patients, and there was one conversion to open surgery (conversion rate, 4.3%). There were no significant differences in estimated blood loss or operative time between LgPCC and SmPCC. No serious perioperative complications occurred, and there was no perioperative mortality.

Conclusion: LA for PCC, including large tumors, is safe, feasible, and effective with appropriate perioperative hemodynamic control.

Key words: adrenalectomy, laparoscopic surgery, pheochromocytoma

Introduction

Pheochromocytoma (PCC) is a rare tumor (incidence $< 0.2\%$ among people with hypertension)¹ that arises from chromaffin cells of the neural crest and typically originates from the adrenal medulla. Although the presentation of these tumors is highly variable, secretion of catecholamine from the tumors gives rise to the classical triad of symptoms: palpitations, headaches, and sweating lasting from minutes to hours and occurring periodically on different occasions.²

The only definitive treatment for PCC is operative resection. Since laparoscopic adrenalectomy (LA) was first described,^{3,4} this minimally invasive procedure has been the modality of choice for removal of benign lesions of the adrenal gland. However, there have been reservations about the utility of LA for PCC, owing to concerns about adverse hemodynamic sequelae resulting from pneumoperitoneum, gland manipulation, and the technical challenges involved in removing these highly vascular tumors.⁵ Despite these reservations, some recent studies demonstrated the feasibility of LA for PCC and

have compared it with the traditional open approach in Western countries.^{6,7} In the present study, we assessed LA for PCC in terms of perioperative outcomes and efficacy in Japanese patients.

Patients and Methods

All demographic, clinical, and operative data were retrieved from a prospectively maintained laparoscopic surgery database at our institution. Twenty-three patients who underwent LA between April 1999 and November 2013 and were diagnosed with PCC upon postoperative histopathological examinations were included in the current study (Table 1). The median age was 52 years at the time of the operation, and 12 (52.2%) of the patients were female. Patients were divided into two groups according to the preoperative tumor size: the ≥ 60 -mm (large PCC, LgPCC) group and the < 60 -mm (small PCC, SmPCC) group.

Each patient underwent clinical and biochemical assessment before surgery. Complete endocrine evaluation and imaging studies, including computed

Received 22 September 2014, accepted 31 October 2014

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tomography and/or magnetic resonance imaging and a metaiodobenzylguanidine scan, were performed on all patients. Elevations in urine adrenaline and noradrenaline levels were calculated as multiples of the upper limit of the normal range. Urine adrenaline or noradrenaline levels greater than three times the upper limit of the normal range were considered diagnostic for PCC, according to the Japan Endocrine Society criteria. All patients received alpha-adrenergic blockade for at least 2 weeks prior to surgery, followed by beta-blockers, if needed, and volume expansion.

Table 1. Demographic and clinical variables

n	23
Male : Female	11 : 12
Median age (range), years	52 (19–78)
Body mass index (kg/m ²)	21.6 (16.0–28.6)
Tumor location	
Right : Left	14 : 9
Surgical approach	TA
Tumor size (range), mm	41 (15–85)
EBL (range), ml	30 (0–1,420)
OR time (range), min	170 (120–545)
Hospital stay (range), days	5 (4–13)
Conversion to open (%)	1 (4.3)
Blood transfusion	None

TA, transperitoneal approach; EBL, estimated blood loss; OR, operative

Surgical procedure

All patients underwent general anesthesia. Arterial catheter for continuous arterial blood pressure monitoring was used. LA was performed by means of a transperitoneal approach in all patients. Patients were placed in the lateral decubitus position and a pneumoperitoneum was established to a pressure of 8–10 mmHg. Three to 4 (12, 10, 5, and 5-mm) trocars were used. In right adrenalectomy, the second 5-mm trocar was inserted on the breast line at the rib margin to retract the liver if needed. The adrenal vein was ligated early in the procedure after the tumor was partially mobilized. Specimens were extracted intact within a bag for pathology.

Statistical analysis

Statistical analysis was performed using two-tailed Student's *t*-tests or analysis of variance with StatView 5.0 software (SAS Institute, Cary, NC, USA). A *P* value of <0.05 was considered to indicate statistical significance.

Results

Of the 23 patients, there were 22 successfully completed LAs, and the LA in one was converted to an open surgery (conversion rate, 4.3%). The median size of the adrenal tumors was 41 mm, and 60% of the tumors were on the right side. Median estimated blood loss (EBL) and

Table 2. Association between tumor size and perioperative outcomes

Variable	SmPCC (<60 mm)	LgPCC (≥60 mm)	<i>P</i> value
n	18	5	-
Male : Female	9 : 9	2 : 3	0.69
Median age (range), years	54.5 (36–74)	49 (19–78)	0.05
Body mass index (kg/m ²)	22.3 (16–28.5)	20.4 (18.4–23.5)	0.17
Tumor location			
Right : Left	10 : 8	4 : 1	0.32
Tumor size (range), mm	40 (15–59)	71 (60–85)	<0.01
EBL (range), ml	25 (0–820)	40 (20–1420)	0.12
OR time (range), min	172.5 (120–290)	150 (120–545)	0.11
Hospital stay (range), days	5 (4–13)	6 (4–10)	0.73
Conversion to open	0	1	-
Elevated urine catecholamine			
Adrenaline (range), fold change	1.0 (0.1–23.1)	29.5 (9.0–47.3)	<0.01
Noradrenaline (range), fold change	1.8 (0.4–28.1)	4.41 (2.6–23.3)	0.02
Incidence of intraoperative hypertension	7	3	0.40
Incidence of intraoperative hypotension	18	5	-

operative (OR) time for all cases were 30 ml and 170 minutes, respectively (Table 1). The one patient who was converted to open surgery had an 85-mm tumor so was in the LgPCC group. The reason for the conversion to open surgery was the inability to obtain adequate exposure owing to severe adhesion. Although the median postoperative hospital stay was 5 days, this particular patient remained in the hospital for 10 days but suffered no long-term sequelae after being discharged.

The LgPCC cohort was comprised of 5 patients (21.7%), and the SmPCC cohort was comprised of 21 patients (72.3%) (Table 2). There were no differences in age, gender, or tumor location between the two cohorts. The percentages of patients with diagnostic elevations in urine adrenaline or noradrenaline in the LgPCC group were significantly higher than the corresponding percentages in the SmPCC group ($P < 0.01$ and $P = 0.02$, respectively). However, intraoperative hemodynamic parameters did not differ significantly with respect to tumor size. Intraoperative hypertensive episodes (systolic blood pressure (BP) ≥ 180 mmHg and/or diastolic BP ≥ 110 mmHg) occurred with comparable frequency in both groups (60%, LgPCC; 38.9%, SmPCC, $P = 0.40$). No paroxysmal hypertension crisis was observed in either cohort. Intraoperative hypotensive episodes (systolic BP ≤ 90 mmHg and/or diastolic BP ≤ 60 mmHg) were recorded in all 23 patients. There were no differences in EBL or OR time between the two groups.

There were no serious perioperative complications, such as a need for blood transfusions or cardiovascular events, or mortalities, and no major postoperative complications reported during the follow-up period, such as ileus or pneumonitis.

Discussion

Surgical manipulation of PCC, which are generally vascularized tumors, is known to cause the excessive release of catecholamine from tumors, and the amount of released catecholamine is in general positively correlated with tumor size.⁸ The additive effects of the catecholamine surge and pneumoperitoneum during laparoscopy may increase the intraoperative risk of hemodynamic instability.^{9,10} Therefore, although LA is recognized as the best modality for the resection of adrenal tumors, it was initially considered as contraindicated for PCC in general and for large PCC in particular. However, some investigators reported results suggesting that LA is a safe and efficient modality for PCC.^{6,7} In the present study, we investigated the perioperative outcomes of laparoscopic resection for both large and small PCC.

In the present series, we found that the incidence of diagnostic elevation in urine catecholamine levels was significantly higher in the LgPCC group than that in the SmPCC group, as indicated by the preoperative endocrine evaluation. However, LA for PCC was performed safely and completely irrespective of tumor size. There were no significant differences in EBL or OR times between the two cohorts. The incidence of intraoperative hypertension episodes was higher in the LgPCC group than that in the SmPCC group but was not statistically significant. Several studies have demonstrated that tumor manipulation is the most significant intraoperative stimulus for catecholamine release.⁹⁻¹¹ Dickson et al. reported that the transperitoneal approach requires lower carbon dioxide insufflation pressures compared with the retroperitoneal approach and results in decreased intraoperative hypertension.¹² Furthermore, early adrenal vein ligation is considered important to reduce the risk of excessive catecholamine excretion.^{13,14} Abbou et al. reported that ligating the adrenal vein before manipulating the gland enabled them to reduce the number of cardiovascular complications.¹⁵

In the present study, we performed transperitoneal LA using relatively low-pressure pneumoperitoneum (8–10 mmHg). The transperitoneal approach has the advantages of a wider working space and readily identifiable anatomic landmarks. These advantages allowed us to minimize gland manipulation and to ligate the adrenal vein earlier. These surgical concepts and modalities may help to maintain hemodynamic stability during surgery even for LgPCC. There were no paroxysmal hypertension crises observed in the present study. Carter et al. reviewed 25 patients who underwent LA for PCC (including 11 large tumors) by means of the same surgical concepts and modalities and found no significant differences in operative hemodynamic stability with respect to tumor size.¹⁶ Wu et al. reported that ligation of the adrenal vein frequently results in a sudden drop in BP.¹⁷ We observed intraoperative hypotension in all the patients in the present study; however, those hypotensive events were not severe and successfully managed with intravenous fluids. However, regardless of the surgical approach, appropriate preoperative preparation, close intraoperative hemodynamic monitoring and management, and meticulous surgical technique are required to optimize patient outcomes.¹²

It has been suggested that a large PCC size is associated with increased risk of malignancy.^{2,18} Although many surgeons have traditionally used a PCC size greater than 60 mm as a contraindication for LA,⁷ there have been some reports of laparoscopic resection of PCC

exceeding 100 mm in size.^{19,20} Nevertheless, among all adrenal tumors, PCC are most likely to result in conversion during LA.²¹ Common reasons for conversion include bleeding and intraoperative suspicion of malignancy as indicated by dense adhesions and loss of planes.^{7,21} Patients with imaging features of malignancy such as metastases and invasion of adjacent structures are usually not offered laparoscopic surgery. In our series, although one patient in the LgPCC group was converted to open surgery because of adhesion, histopathology revealed no malignancy. However, especially for large PCC, surgeons should strictly adhere to oncological principles. If an oncological resection cannot be performed during a minimally invasive procedure, conversion to an open procedure should not be delayed.

The main limitations of our study were the small sample size and that it was a retrospective study on a prospective database. The low incidence of large PCC hinders performance of randomized and prospective studies. However, our results indicate that LA for PCC, including large tumors without preoperative suspicion of malignancy, is safe, feasible, and effective, with appropriate perioperative hemodynamic control.

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