Original Article

Laparoscopic Adrenalectomy—Is It Any Different in Phaeochromocytoma and Non-Phaeochromocytoma?

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BACKGROUND: Laparoscopic adrenalectomy (LA) for phaeochromocytoma is a feasible, safe and effective treatment. The effects of associated catecholamine release render LA more challenging, although with comparable morbidity to LA for other diseases of the adrenal gland.
METHODS: Data from case records of 44 patients who underwent LAs between May 2002 and May 2006 were analysed retrospectively. The patients were divided into a phaeochromocytoma group (Group I) and a non-phaeochromocytoma group (Group II). The aim of this study was to assess the operative course and outcome of LA in the two groups.
RESULTS: The mean operating time and blood loss were slightly higher in LA for phaeochromocytomas compared to LA for other pathologies, but these differences were not statistically significant. The mean hospital stay was 3.84 days in both groups. The phaeochromocytoma group had a slightly higher complication rate of 21% compared to 12%. None of the procedures needed open conversion. A terminal hand assist was employed in two patients in Group I and one patient in Group II. Two patients with bilateral phaeochromocytoma had single stage bilateral LA.
CONCLUSION: LA is feasible and effective in phaeochromocytoma. It is associated with a slightly longer operating time, more blood loss and complications when compared with non-phaeochromocytoma masses. LA can be done in a single operation for bilateral masses. Terminal hand assist is a viable and effective option for very large masses. [*Asian J Surg* 2007;30(4):244–9]

Key Words: adrenal cortical adenoma, adrenal gland neoplasm, adrenalectomy, catecholamine, laparoscopy, phaeochromocytoma

Introduction

Since its first description in 1992, laparoscopic adrenalectomy (LA) has become the gold standard for adrenal surgery.[1] LA in phaeochromocytoma has received considerable attention in view of the haemodynamic alterations resulting from the pneumoperitoneum and manipulations during surgery. This was our endeavour to determine whether the outcome of LA was any different in phaeochromocytoma as compared to other lesions.

Methods

Prospectively entered data of patients who underwent LA between May 2002 and May 2006 were analysed. The results of LA for phaeochromocytoma were then compared with LA for adrenal lesions other than phaeochromocytoma, assessing the operative course and outcome of LA in the two groups. Group I (phaeochromocytoma group) included 19 patients while group II (non-phaeochromocytoma group) had 25 patients with adrenal pathologies other than phaeochromocytoma.

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All patients underwent preoperative imaging by contrast-enhanced computed tomography and biochemical evaluation, which included estimation of 24-hour urinary vanillylmandelic acid (VMA), cortisol and metanephrines. Metaiodobenzylguanidine scanning, iodonorcholesterol scanning and magnetic resonance imaging were done in selected patients. All masses found to be functional on biochemical assay were adequately prepared preoperatively. Phaeochromocytomas were prepared by adequate volume replacement and control of hypertension with alpha blockade and beta blockade, if needed. Alpha-blockers were started 1 week prior to surgery or if the patient developed hypotension, at a dose of 1 mg of doxazosin and titrated up to 2 mg. Patients with Conn's syndrome received oral potassium supplementation and spironolactone.

A single surgeon (HSB) performed the procedures using the lateral transabdominal approach. Three ports were used on the left side and four on the right with the patient in the lateral decubitus kidney position. By an open Hasson's technique, a 10-mm camera port was inserted 2 cm above the umbilicus at the lateral border of the rectus sheath. Two working ports were used in the midclavicular line, a 10-mm port in the iliac region 5 cm medial to the anterior superior iliac spine and a 5-mm port subcostally. An additional 5-mm epigastric port was used for liver retraction on the right side. Carbon dioxide was used for insufflation maintaining a pneumoperitoneal pressure of 12 mmHg.

On the left side, early control of the adrenal vein at its origin from the renal vein was attained after colonic and splenopancreatic mobilization. On the right side, the adrenal vein was exposed at the superomedial border of the gland after mobilizing the right lobe of the liver and exposing the subhepatic inferior vena cava. After control of the adrenal vein with ligaclips, the gland was removed using the Harmonic Scalpel™ (Johnson & Johnson Ethicon Endo Surgery Inc., Cincinnati, OH, USA). Specimens were retrieved after extending one of the port incisions. In two cases with large masses, a midline epigastric incision was used for terminal hand assist (technique described in results section) and retrieval. The specimen was retrieved through an existing tubectomy scar in a female who underwent bilateral single stage adrenalectomy for multiple endocrine neoplasia (MEN) 2A syndrome. In all the others, the specimens were removed intact without morcellation in an endo-catch bag.

The mean (95% confidence interval of mean lower and upper bound) operating time, mean blood loss and hospital stay in the two groups were assessed by statistical analysis using SPSS version 11 (SPSS Inc., Chicago, IL, USA). The statistical test used was the independent sample *t* test. Intraoperative haemodynamic alteration was defined as a rise in systolic blood pressure by 30% and/or diastolic pressure by 10% of baseline at any time from positioning, induction, creating pneumoperitoneum and handling the tumour. A fall in blood pressure by the same margins after removal of the tumour was also considered as haemodynamic alteration.

Results

Fifty-two LAs were done in 44 patients. These included 30 females and 14 males with a mean age of 38.43 years (range, 1–73 years). Final histopathology in 19 patients showed phaeochromocytoma while 25 had other pathologies. Eight patients underwent bilateral single stage LA (phaeochromocytoma, $n = 2$; Cushing's disease, $n = 6$). Single stage bilateral LA for phaeochromocytoma was performed in one female with MEN 2A syndrome and another young boy with bilateral adrenal masses.

In the phaeochromocytoma group, mean age ± standard deviation was 33.79 ± 13.72 years. Ten of the masses were on the right side, seven on the left side and two were bilateral. The mean size (95% confidence interval of mean lower and upper bound) of masses, operating time and blood loss were 6 (5.11, 6.94) cm, 129.58 (100, 159) minutes and 79.74 (43, 116) mL, respectively (Tables 1 and 2).

In the non-phaeochromocytoma group, the mean age of the patients was 41.9 ± 16.68 years. Of these, there were nine on the left and 10 on the right side. Six patients with Cushing's disease underwent bilateral single stage LA. The mean size of the masses was 5.06 (4.4, 5.7) cm. Mean operating time was 103 (82.7, 124.4) minutes and mean blood loss was 48 (25, 71) mL.

Using the independent sample *t* test, the differences between various parameters in the two groups were not found to be statistically significant.

The final histopathology of the masses is shown in the Figure. A normal adrenal gland was removed in a teenage boy with uncontrolled hypertension, which required three drugs. His urinary VMA was elevated and a computed tomography scan was misinterpreted to show a left adrenal mass. In retrospect, this occurred because a prominent splenic notch was interpreted as an adrenal adenoma.

Table 1. Demographics of phaeochromocytoma (P) and non-phaeochromocytoma (Non P) masses

Study	Adrenal units (*n*)		Approach		Mean size (cm)		Hospital stay (d)	
	P	Non P	P	Non P	P	Non P	P	Non P
Kalady[15]	28	27/19*	NA	NA	NA	NA	3.4	–
Gotoh[16]	9	28	LTA	LTA	5.4	2.4	NA	NA
Kim et al[17]	26	34	NA	NA	4.9	2.7	4	2
This study	21	31	LTA	LTA	6	5	3.9	3.8

*Aldosteronoma/incidentaloma. NA = not applicable; LTA = lateral transperitoneal approach.

Table 2. Operative parameters of phaeochromocytoma (P) and non-phaeochromocytoma (Non P) masses

Study	Blood loss (mL)		Complications (%)		Conversion (%)		Operating time (min)	
	P	Non P	P	Non P	P	Non P	P	Non P
Kalady[15]	150	88/75*	10.8	–	10.8	–	171	171
Gotoh[16]	360	54	25	NA	11	NA	199	177
Kim et al[17]	276	196	23	8.8	3.8	2.9	191	162
This study	79.7	48	21	12	2 THA	1 THA	129.5	103

*Aldosteronoma/incidentaloma. NA = not applicable; THA = terminal hand assist.

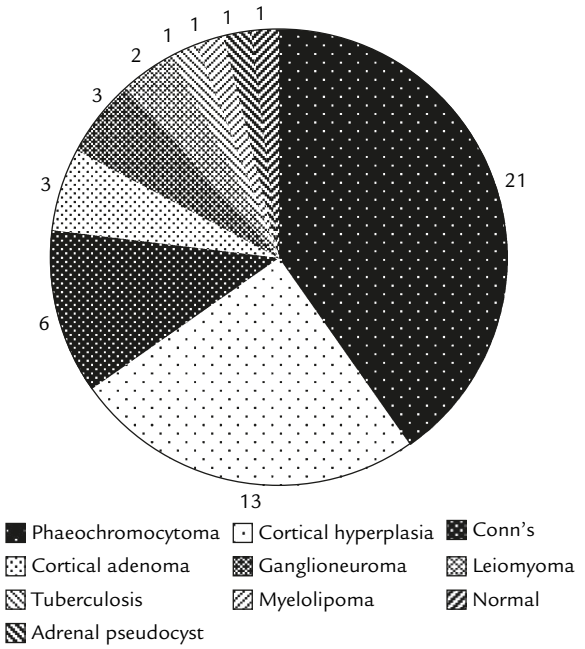

Figure. Histopathology of the lesions: type and number in 52 adrenal units.

Of the 19 patients in the phaeochromocytoma group, 16 had hypertension preoperatively. Blood pressure resolved with surgery alone in 12 patients (75%) and came under control with a single drug in the remaining four patients. In group II, 21 patients were hypertensive. Five patients with Conn's syndrome were cured after surgery.

Fifteen out of the 19 patients (78.9%) with phaeochromocytoma had significant intraoperative alterations in blood pressure. Three of these patients developed severe hypertension during all stages of operation including positioning, creation of pneumoperitoneum and tumour dissection. Pneumoperitoneum *per se* did not result in significant haemodynamic alterations in the other 11 patients. The rise in blood pressure was adequately managed by interruption of the procedure and sodium nitroprusside infusion. Early venous control was aimed at in all patients. All 15 patients had hypertension on handling the tumour. Later, five of the patients developed hypotension for less than 12 hours which required volume replacement in two and a pressor agent (dopamine) in three. None of the patients in the non-phaeochromocytoma group showed any rise in blood pressure.

A complication rate of 21% (4/19) was seen in the phaeochromocytoma group. Three patients developed pulmonary oedema. Two of these resulted from intraoperative haemodynamic alterations with fluid overload and required postoperative ventilation for 8 hours. The third occurred in a 72-year-old female with coronary artery disease, who developed pulmonary oedema due to myocardial ischaemia

on the second postoperative day. She was managed conservatively. One patient with a large adherent phaeochromocytoma required transfusion to replace intraoperative blood loss.

The non-phaeochromocytoma group had a complication rate of 12% (3/25). This included one patient with transient fever secondary to a subhepatic collection. This patient had undergone concomitant de-roofing of a renal cyst. One patient with a large tuberculous mass required a blood transfusion and one patient with a large myelolipoma developed infection of the incision. All these complications resolved with conservative measures alone.

Terminal hand assist (THA), not amounting to open conversion, was employed in two patients with large vascular phaeochromocytomas in whom the procedure could not be safely completed purely laparoscopically. In one patient with a large left-side 11-cm mass, THA was done through a midline supraumbilical incision. The second indication was in a child with bilateral phaeochromocytomas (5 cm on the left and 8 cm on the right). After complete laparoscopic excision of the left-side mass, the right-side tumour was extracted with a hand inserted through a Pfannensteil incision towards the end of the procedure. This was necessary because of the size, large collateral vessels and retrocaval extension of the mass. In group II, one patient with a large tuberculous gland that was densely adherent (9 cm) required THA. No special hand port device was needed for these procedures as they were carried out for a very short period of time towards the end of the operation. Loss of pneumoperitoneum could be adequately reduced with manual compression around the incision through which the hand was snugly inserted.

Discussion

LA has become the approach of choice for the management of phaeochromocytoma.[2] The incidence of haemodynamic changes occurring during LA and open adrenalectomy (OA) for phaeochromocytoma have been reported to be similar.[2] In fact, some studies have reported that the episodes of haemodynamic instability with LA in phaeochromocytomas have been observed to be equal to or lesser than those observed during open surgery.[3–6] This could be because there is minimal handling of the tumour with early control of the adrenal vein in LA in comparison to OA. Although studies have shown that the late ligation of the adrenal vein, as happens in the retroperitonoscopic approach, does not affect the occurrence of hypertensive episodes, it is felt that adequate preoperative alpha-receptor blockade prevents these episodes.[7–9] In our study, intraoperative hypertensive events were seen in the majority of patients (78.9%, 15/19) with phaeochromocytoma at various times during surgery, in spite of adequate preoperative preparation with alpha blockade and, when necessary, beta blockade. In some cases, these episodes persisted even after adequate control of the main adrenal vein, probably due to catecholamine release through accessory adrenal veins or collaterals. Although these haemodynamic alterations were frequent, they could be controlled relatively easily and quickly with drugs or temporary interruption of the procedure. Postoperative hypotension seen in a few patients could be managed with volume replacement and pressor agents.

Many approaches to LA have been described. We prefer the lateral transperitoneal approach (LTA) as the working space is greater, exposure is good and larger masses can be dealt with easily. Early control of the adrenal vein can also be achieved with minimal manipulation of the tumour with this approach. According to Janetschek et al, retroperitoneal endoscopic adrenalectomy (REA) did not offer any clear advantage over LTA.[3] Technically, it is often not possible to approach the adrenal vein first by REA. For obvious reasons, REA is preferable in patients who have undergone previous laparotomy in the area of interest.

Whether CO_2 insufflation and intra-abdominal pressure may contribute to haemodynamic alteration during LA for phaeochromocytomas has been an area of concern. In general, prolonged laparoscopic surgery with CO_2 may induce cardiac arrhythmias due to acidosis-induced release of catecholamines, especially in elderly patients. It is generally also observed that when effective ventilation techniques and monitoring are applied, hypercarbia and hypoxia are rarely encountered. Maintaining intra-abdominal pressure less than 12 mmHg is recommended by most studies.[10] The hypertensive response during the induction of pneumoperitoneum in phaeochromocytoma patients is not significant and can be managed easily with antihypertensive drugs. It is in fact the tumour manipulation that causes the greatest rise in plasma catecholamine levels.[11–13] Clinically significant haemodynamic alterations during tumour manipulation were more commonly encountered during conventional OA than during LA.[13] It has been suggested that a low intra-abdominal pressure of 8–10 mmHg causes less catecholamine release and fewer haemodynamic

fluctuations.[14] Helium pneumoperitoneum has been tried with good results, although randomized controlled trials comparing helium and CO_2 are not available.[11,13] In our study, CO_2 was used and all procedures were completed satisfactorily. We did not study catecholamine levels and different pneumoperitoneal pressures.

The results of the present series in terms of operating time, blood loss, conversion rates, complication rates and hospital stay compare favourably with other large series[15–17] (Table 2).

Gagner et al have reported greater complications in phaeochromocytomas as compared to other lesions probably due to their larger sizes and haemodynamic alterations. They concluded that LA is the procedure of choice in phaeochromocytoma although it is associated with more complications than LA for other lesions.[18] The only major complication faced in the present series was transient pulmonary oedema, probably due to the haemodynamic alterations and fluid shifts associated with their correction.

For large tumours, size makes dissection difficult and time-consuming with a consequent increase in complications; in such cases, it may be prudent to employ hand assistance.[19] Due to cost constraints, we employed THA laparoscopy (without any special hand port device) as an effective variant of minimal access surgery. This approach permitted successful completion of surgery for large and adherent tumours (two phaeochromocytomas and one tuberculous gland).

There are reports of recurrence following LA for large phaeochromocytomas. These have occurred in malignant lesions and when fragmentation of the tumour during handling occurred.[7,8] In the present series, we did not experience rupture or recurrence in spite of four tumours being larger than 8 cm. Longer follow-up may indicate the true recurrence rates.

The 75% resolution rate of hypertension in our series of phaeochromocytomas corresponds with that mentioned in the literature (70–100%).[3,6,7,11] The patients with persistent hypertension were easily managed with one antihypertensive medication. All patients with aldosteronomas were successfully treated for hypokalaemia. One of the six patients (16.7%) with Conn's adenoma in our series had persistent hypertension. A review of the literature indicates a 12–34% persistence of hypertension (probably due to long-standing hypertension, age, family history of hypertension and coexisting essential hypertension).[20,21]

LA has become the gold standard treatment for adrenal masses. LA can be safely and effectively performed in phaeochromocytoma. The advantages of low morbidity, fewer complications and quick recovery, along with cure of hypertension and lack of hormonal recurrence, make LA an attractive option in phaeochromocytoma. However, it may be associated with slightly increased blood loss, operating time and complication rates when compared to LA for other adrenal pathologies. It can be performed safely, bilaterally, and in a single stage in patients with bilateral phaeochromocytoma when adequate expertise is achieved. It is wise to consider a hand-assisted procedure when the mass is large, adherent, hypervascular and has retrocaval extension.

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