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SURGICAL ENDOSCOPY
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Laparoscopic adrenalectomy for pheochromocytoma

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Abstract

Background: Laparoscopic adrenalectomy for Conn's syndrome, Cushing's disease, cortisol-producing adenomas, and nonfunctioning adenomas has been well established. This study was intended to evaluate the clinical outcomes of patients undergoing laparoscopic adrenalectomy for pheochromocytoma, and to assess the efficacy and safety of a minimally invasive approach.

Methods: Data were collected prospectively on all patients undergoing laparoscopic adrenalectomy for pheochromocytoma over a 5-year period.

Results: In this study, 39 consecutive patients underwent laparoscopic resection of a pheochromocytoma: 38 adrenal (23 left, 15 right) and 1 extraadrenal paraganglioma. There were no conversions to open surgery. The mean tumor size was 5.2 cm (range, 2–12.1 cm). Average operative time was 159 min (range, 100–265 min), and average estimated blood loss was 72 ml (range, 30–350 ml). Intraoperative hypertension (systolic blood pressure > 170 mmHg) occurred in 67% of the patients, and hypotension (systolic blood pressure < 90 mmHg) in 39% of the patients. The mean length of stay was 2.1 days (range, 1–4 days). There were three minor postoperative complications. During a mean follow-up period of 14 months, there were no mortalities or recurrences of endocrinopathy.

Conclusions: Laparoscopic resection of pheochromocytomas can be accomplished safely despite frequent episodes of hemodynamic variability equal to those of historic open control subjects. A short hospital stay with expedient recovery,minimal wound complications, and lack of endocrinopathy recurrence makes a minimally invasive approach the procedure of choice for the management of pheochromoctyoma.

Key words: Laparoscopic adrenalectomy — Pheochromocytoma — Minimally invasive surgery

The safety and efficacy of laparoscopic adrenalectomy for functional and nonfunctional tumors of the adrenal glands are well-documented [2, 4]. As with other minimally invasive procedures, laparoscopic adrenalectomy is associated with less postoperative pain, shorter length of stay, fewer complications, and more rapid convalescence than the open approach [6, 10]. Laparoscopic resection of pheochromocytomas is feasible but potentially more challenging because of the risks for intraoperative hemodynamic variability and the frequent larger size of these tumors. Even in experienced hands, laparoscopic adrenalectomy for pheochromocytoma has been associated withlonger operative times, increased complications, and longer hospitalizations than for other adrenal pathologies [3]. In this report, we describe the largest consecutive series of laparoscopic resections for pheochromocytoma.

Patients and methods

From January 1995 to February 2000, 39 consecutive patients underwent laparoscopic resection of a pheochromocytoma: 38 adrenal (23 left, 15 right) and 1 extraadrenal paraganglioma. Data were collected prospectively and included demographics, operative indications, tumor size, and location. Operative details including blood loss, operative time, hemodynamic parameters, complications, length of stay, and response to therapy were analyzed.

Preoperative diagnosis of pheochromocytoma was based on clinical, biochemical, and radiographic evaluation. Of the 39 patients, 37 presented with hypertension and elevated urinary metanephrine levels. Tumors were located by computed tomography (CT), T2-weighted magnetic resonance imaging (MRI), or both. An assessment of family history, a thorough physical examination, and serum calcium and calcitonin levels were obtained for all patients to rule out multiple endocrine neoplasia. In two cases, adrenalectomy was performed for an adrenal mass in the absence of preoperative biochemical abnormalities or hypertension. Intraoperative findings and histology led to the diagnosis of pheochromocytoma.

In the 37 patients with preoperative signs and symptoms of catecholamine excess, alpha-adrenergic blockade was initiated at least 10 days before surgery. Normalization of blood pressure was defined as a resting blood pressure lower than 160/90 mmHg. For patients with coexisting tachycardia, beta-blockade was added. Patients with orthostatic hypotension were treated with oral, intravenous volume loading, or both during the days before surgery. Patients were infused with 2 l of crystalloid solution for intravascular volume expansion before the induction of anesthesia.

Adrenalectomies were performed via a transperitoneal, lateral laparoscopic approach using three or four subcostal ports, as previously described [5]. The extraadrenal pheochromocytoma was removed using four ports placed in the midabdomen [7]. An arterial line was used for continuous intraoperative blood pressure monitoring in all cases. Intravenous vaso-

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Table 1. Comparison of laparoscopic and open adrenalectomy for pheochromocytoma

	Ulchaker [12] (n = 113)	Mobius [9] (n = 9)	Mobius [9] (n = 9)	Gagner [3] (n = 23)	Current Study (n = 39)
Approach	Open	Open	Laparoscopic	Laparoscopic	Laparoscopic
Tumor size (cm)	6 (1.8–22)	4.5 (3–7)	3.8 (1.7–7.5)	6.3 (mean)	5.2 (2–12.1)
Operative time (min)	NR	100 (85–130)	243 (125–360)	230 (180–360)	159 (100–265)
Intraoperative hypertension (%)	94	78	88	59	67
Intraoperative hypotension (%)	NR	NR	NR	53	39
Estimated blood loss (ml)	NR	NR	NR	NR	72 (30–350)
Transfusion (%)	NR	44	NR	NR	0
Conversions (%)	—	—	22	—	0
Morbidity					
Major (%)	5.3	0	11	22	2.6
Minor (%)	58	0	0	0	5.0
Mortality	0	0	0	0	0
Length of stay (days)	8.9 (3–44)	10 (8–13)	6 (4–9)	8.4 (mean)	2.1 (1–4)

NR, not reported

pressors and vasodilators were prepared before the induction of anesthesia. Intraoperative hypotension was defined as a systolic blood pressure (SBP) lower than 90 mmHg and treated with a combination of volume infusion and pressors at the discretion of the attending anesthesiologist. Hypertension was defined as a systolic blood pressure higher than 170 mmHg managed with acombination of intravenous vasodilators (nitroprusside) and short-acting beta-blockers (esmolol) as well as transient cessation of tumor dissection, abdominal desufflation, or both. Care was taken in all cases to avoid excessive manipulation of the adrenal gland or penetration of the capsule. When possible, early ligation and division of the adrenal vein was performed. Standard 5-mm and 10-mm laparoscopic instrumentation was used for all cases. Control of exceptionally large capsular vessels and large adrenal veins was obtained with laparoscopic clips or a linear vascular stapler. Specimens were placed into an impervious extraction bag before morcellation and removal.

Results

Laparoscopic adrenalectomy for pheochromocytoma was performed in 38 patients. One additional patient successfully underwent surgery for an extraadrenal pheochromocytoma arising from the organ of Zuckerkandl. Altogether, the study involved 14 men and 25 women with a mean age of 43 years (range, 19–59 years). The mean tumor size was 5.2 cm (range, 2–12.1 cm). Four patients had multiple endocrine neoplasia syndrome. In two of these patients, a primary diagnosis of medullary thyroid carcinoma resulted in an endocrine workup and identification of a pheochromocytoma. Both patients underwent laparoscopic adrenalectomy before thyroidectomy.

The operative time in all cases averaged 159 min (range, 100–265 min). The mean estimated blood loss was 72 ml (range, 30–350 ml). There were no conversions to open surgery. Intraoperative hypertension occurred in 26 patients (67%). All were controlled with intravenous vasodilators and transient cessation of tumor manipulation. Intraoperative hypotension occurred in 15 patients (39%). Each responded to volume infusion, pressor agents, or both. In one patient, postoperative hypotension related to residual alpha-blockade developed, which responded to volume resuscitation. There were no ventricular arrhythmias, and no patient required transfusion.

The mean length of stay was 2.1 days (range, 1–4 days). There were three perioperative complications. One case of wound cellulitis and one urinary tract infection were managed with oral antibiotics. In one patient developed a lower extremity deep venous thrombosis with micropulmonary emboli developed 8 days postoperatively. A hypercoagulability evaluation yielded negative results, and the patient was treated with oral anticoagulation. There were no mortalities.

Histologic evaluation identified pheochromocytoma in all cases, none of which were malignant.

Follow-up evaluation for all the patients included blood pressure monitoring at monthly intervals for the first year, then yearly thereafter. Urinary metanephrine levels were followed annually for a period of 5 years. Follow-up abdominal imaging was obtained only in the patients with recurrent hypertension or elevated metanephrines. At a mean follow-up period of 14 months (range, 1–40 months), there were no recurrences of endocrinopathy. Three patients (7.7%) had mild, persistent hypertension that was medically controlled. Biochemical evaluation and repeat CT scans of the abdomen for tumor recurrence produced negative results. There were no long-term wound complications or hernias.

Discussion

Whether performed by an open procedure or laparoscopically, life-threatening complications can occur during pheochromocytoma resection. With advances in preoperative management, tumor location, and anesthesia care, reported mortality rates currently range from 0% to 3.8%, with major complications occurring in 5% to 22% of patients [3, 12, 13]. In most cases, morbidity and mortality stem from intraoperative hemorrhage, hemodynamic instability, or ventricular dysrhythmias [8]. Pheochromocytomas also carry a malignant potential, and frequently are larger than other functional adrenal tumors. Both possibilities have been proposed as a potential contraindication to laparoscopic resection [1]. As a result, laparoscopic adrenalectomy for pheochromocytoma has been viewed with some concern, and there have been few reported studies as of this writing.

Regardless of the anatomic location or surgical approach, resection of catecholamine-producing tumors requires careful preoperative and intraoperative management. Adequate blood pressure control and volume expansion should be achieved with alpha- and/or beta-blocking agents over several weeks before surgery. Despite these measures, intraoperative release of catecholamines can cause rapid

swings in blood pressure. Continuous invasive monitoring and pharmacologic intervention by a skilled anesthesia team is necessary to avoid substantial cardiovascular instability. At the same time, the surgeon must avoid excessive tumor manipulation, which can result in catecholamine surges.

In 1996, Gagner et al. [3] reported their experience with 23 laparoscopic adrenalectomies for pheochromocytoma. Intraoperative hypertension (SBP > 200 mmHg) occurred in 58% of patients, with hypotension (SBP < 80 mmHg) occurring in 53% of cases. This compares favorably with open series reports of hypertensive episodes in as many as 75% of patients [13]. In case-control studies, other authors have confirmed that there are no significant differences in intraoperative hemodynamic changes between laparoscopic and open surgery for pheochromocytoma [9, 14].

Using slightly more stringent criteria for hemodynamic variability (SBP > 170 mmHg or <90 mmHg), our data are consistent with those of other investigators. In our patients, alpha-blockade was used in all patients with preoperative evidence of catecholamine excess. Intraoperative hypertension occurred in 67% of the cases, with 39% of the patients experiencing transient intraoperative hypotension. None experienced adverse effects, and there were no ventricular arrhythmias. Although the use of calcium channel blockers for preoperative blood pressure control has been advocated, we have not had experience with this form of antihypertensive therapy [12].

In addition to the potential problems associated with catecholamine liberation, the increased size, prominent vascularity, and dense adherence of pheochromocytomas to adjacent vessels adds to the difficulty of removing these tumors. As a result, both laparoscopic and open approaches to these tumors have been associated traditionally with higher complication rates than adrenalectomy for other indications. In a recent study of 113 open resections, the overall morbidity rate was 62%, with 5.3% of the patients experiencing a major complication [12].

Laparoscopic studies have reported similar complication rates, ranging from 11% to 22%, with conversion rates of 20% in several studies. Perioperative blood transfusions exceeding 10% for laparoscopic adrenalectomy and 40% for open surgery have been reported recently [9, 14]. Laparoscopic resection of pheochromocytomas has been associated with longer operative times, higher complication rates, and longer hospitalization than that for other adrenal tumors [3].

In the current study, operative time, blood loss, complications, and length of hospital stay compare favorably with those in other reports of laparoscopic and open adrenalectomy for pheochromocytoma (Table 1) [3, 9, 12]. There were no mortalities, no transfusions, and no conversions. We believe that these results relate to a combination of factors including adequate preoperative alpha-blockade, careful intraoperative anesthesia management, and perhaps most importantly, increasing operative experience with laparoscopic adrenalectomy. As demonstrated by other authors, the learning curve may play a significant role in improving the efficiency and safety of advanced laparoscopic procedures [11, 14]. With continued experience, the standardization of this technique in the setting of smaller, nonfunctional tumors has contributed significantly to surgeons' comfort in managing larger, catecholamine-producing tumors.

Although there are no absolute contraindications based on tumor size, lesions larger than 12 cm should be approached cautiously. We have not identified a higher incidence of intraoperative hypertension with larger tumors, although laparoscopic manipulation of these lesions is inherently more difficult. More importantly, larger tumors frequently will encroach on the renal vessels. These structures must be carefully protected to avoid inadvertent injury during dissection.

Up to this time, we have approached all cases of pheochromocytoma laparoscopically. Conversion to an open procedure is warranted when laparoscopic dissection cannot be performed safely, or when there is a concern for malignancy. In the setting of pheochromocytoma, this determination must be based on intraoperative findings of tumor invasion into adjacent structures.

With continued improvements in anesthetic management and operative technique, minimally invasive resection of pheochromocytomas is safe, although technically challenging. Our data suggest that the safety and efficacy of laparoscopic adrenalectomy for pheochromocytoma approach that for other adrenal pathologies.

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