International Braz J Urol

Vol. 35 (1): 24-35, January - February, 2009

Pheochromocytoma: A Long-Term Follow-Up of 24 Patients Undergoing Laparoscopic Adrenalectomy

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ABSTRACT

Purpose: Pheochromocytomas are tumors derived from chromaffin cells that often secrete catecholamines and cause hypertension. The clinical diagnosis of pheochromocytoma depends on the presence of excessive production of catecholamines. Conventional imaging modalities that have been used in the preoperative evaluation include CT, MRI, and 131I-MIBG scintigraphy. Surgical resection is the definitive treatment for patients with pheochromocytoma. The goal of this study was to evaluate the long-term follow-up of 24 patients undergoing laparoscopic adrenalectomy for pheochromocytoma. Materials and Methods: From January 1995 to September 2006, 24 patients underwent laparoscopic adrenalectomy for adrenal pheochromocytoma. Twenty (83.3%) patients had arterial hypertension. The inclusion criteria of patients in this retrospective study were laparoscopic approach, unilateral or bilateral adrenal tumor, pathological diagnosis of pheochromocytoma and a minimum follow-up of 18 months.

Results: Intra-operative complications occurred in 4 (16.7%) patients. Two (8.3%) patients had postoperative complications. Two patients (8.3%) had blood transfusion. The mean postoperative hospital stay was 3.8 days (range 1 to 11). Eighteen (90%) of the twenty patients who had symptomatic hypertension, returned to normal blood pressure immediately after surgery, during the hospital stay. In one patient, the high blood pressure levels remained unchanged. Another patient persisted with mild hypertension, well controlled by a single antihypertensive drug.

Conclusions: Our results confirmed that laparoscopic adrenalectomy for pheochromocytoma is a safe and effective procedure, providing the benefits of a minimally invasive approach. In our study, the initial positive results obtained in the treatment of 24 patients were confirmed after a mean follow-up of 74 months.

Key words: laparoscopy; pheochromocytoma; adrenalectomy **Int Braz J Urol. 2009**; **35**: 24-35

INTRODUCTION

Pheochromocytomas (PCCs) are tumors derived from chromaffin cells that produce and often secrete catecholamines. Over 90% of PCCs are in the abdomen, most frequently in the chromaffin cells of the adrenal medulla. Approximately 10% are found in extra-adrenal sites where they are called paragangliomas due to their association with sympathetic nervous system ganglia in the chest, abdomen, or pelvis (1).

The estimated incidence ranges from 0.005% to 0.1% of the general population and from 0.1% to 0.2% of the adult hypertensive population. The highest incidence occurs during the fourth and fifth decades of life, and is nearly identical in both sexes (1).

Approximately 10% of pheochromocytomas are hereditary. Hereditary tumors are frequently multiple or bilateral and rarely malignant. Familial syndromes associated with PCCs include multiple endocrine neoplasia type 2 (MEN 2), von Hippel-Lindau

disease (VHL), and the neuroectodermal dysplasias consisting of neurofibromatosis, tuberous sclerosis, and Sturge-Weber syndrome (2). Approximately 10 to 15% of pheochromocytomas exhibit malignant behavior. In order to diagnose malignant PCCs, one must document invasion of adjacent organs or metastatic disease. The most frequent sites of metastases are the liver, lung, and bone, particularly the spine, skull, and ribs. There is no absolute clinical, imaging, or laboratory criteria to predict malignancy; however, patients with malignant disease tend to have larger tumors and higher urinary metanephrine levels (2).

Conventional imaging modalities that have been used in the preoperative evaluation of patients with a biochemically confirmed pheochromocytoma include CT, MRI, and Iodine-131-metaiodobenzylguanidine (131 I-MIBG) scintigraphy. CT easily detects tumors of 1 cm or more with high sensitivity, which varies between 93% and 100% for adrenal gland tumor detection and approximately 90% for extra-adrenal disease identification (Figure-1). MRI is also sensitive. Characterization of adrenal masses is done with chemical shift MRI based on the absence of fat in PCCs. In addition, the hypervascularity of pheochromocytomas makes them appear characteristically bright, with a high signal on T2-weighted images (Figure-2). 131I-MIBG scanning works by administering a radiolabeled amine for which chromaffin tissue is selectively avid. Since it is a physiologic study, MIBG can identify pheochromocytomas regardless of their location. This modality may be useful in patients with biochemical evidence of a pheochromocytoma that has not been localized by CT or MRI or in the follow-up evaluation of patients with suspected or documented recurrent or metastatic disease (2).

Surgical resection is the definitive treatment for patients with pheochromocytoma. Prior to the surgery, the patient must be adequately prepared with alpha-adrenergic blockade and complete restoration of fluid and electrolyte balance. Alpha-blockade works to oppose catecholamine-induced vasoconstriction and sometimes must be associated with the beta-adrenergic blockade with propranolol and expanding volume (3).

Pheochromocytoma was initially considered a contraindication to laparoscopic approach due to the fear of hypertensive crisis associated with the pneumoperitoneum. However, an increasing series of laparoscopy using the transperitoneal or retroperitoneal approach have been reported and proved to be a safe procedure with similar blood loss and no difference in blood pressure or heart rate increments when compared with open adrenal ectomy (3). Patients also experience faster resolution of postoperative ileum, decreased analgesic requirements, a shorter length of hospital stay, and a shorter convalescence with a more rapid return to normal activity (3-5).

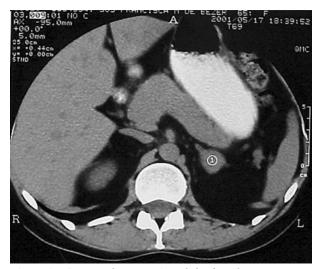


Figure 1 – CT scan showing a 2 cm left adrenal mass.

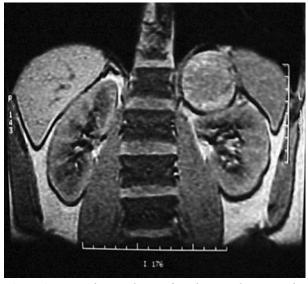


Figure 2 – MRI showing large adrenal mass - hypersignal in T?

The goal of this study was to evaluate the long-term results of 24 patients undergoing laparoscopic adrenal ectomy for pheochromocytoma.

MATERIALS AND METHODS

From January 1995 to September 2006, we retrospectively reviewed the results of transperitoneal laparoscopic adrenalectomy performed in 24 patients with pheochromocytoma. This series consisted of 14 (58.3%) males and 10 (41.7%) females, with the mean age of 46 years (range 10 to 75 years, median 46.5).

The Body Mass Index (BMI) ranged from 19.4 to 33.5. Nine (37.5%) cases presented with overweight (BMI between 25 and 30) and one (4.2%) case with obesity (BMI 33.5).

Twenty (83.3%) of the twenty-four patients had arterial hypertension, half of them with severe hypertensive crisis and the other 10 patients with mild to moderate hypertension. The mean time between installation of hypertension and the diagnosis of pheochromocytoma was 3 years (3 months to 8 years). Four (16.7%) patients had normal blood pressure levels. Three were completely asymptomatic (incidental findings) and 1 had abdominal pain and recurrent anxiety crises.

The mean tumor size estimated by CT scan was 3.9 cm (1 to 12 cm, median 3.7 cm). In 14 (58.3%) patients the tumors were on the right side, 9 (37.5%) on the left, and only 1 (4.2%) was bilateral (Table-1).

The inclusion criteria of patients in this retrospective study were laparoscopic approach, unilateral or bilateral adrenal tumor, pathological diagnosis of pheochromocytoma and a minimum follow-up of 18 months.

The preoperative diagnosis of pheochromocytoma in the symptomatic patients was confirmed by the clinical presentation and the biochemical and radiographic findings. The vanylmandelic acid level of a 24-hour urine sample and plasma norepinephrine and epinephrine levels were routinely tested before surgery and every six months after surgery. Abdominal CT scans were obtained in all cases, both in pre-operative as in the post-operative annually. 131I-MIBG was performed in 21 patients, 20 cases with clinical and laboratory suspicion of pheochromocytoma and one

case without any suspicion that presented an incidental finding. In all cases MIBG were repeated annually after surgery. MRI was performed in 7 patients in the pre-operative evaluation because of iodine allergy or inconclusive CT images.

Patients with hypertension and/or abnormally high catecholamine levels were given prazosin 2 to 20 mg/day during 14 to 21 days before surgery. In order to expand the blood volume, patients were infused with crystal liquids (2 to 3 liters) just prior to surgical intervention. All patients underwent general endotracheal anesthesia. The mean arterial pressure, central venous pressure, and vital signs were monitored during surgery. Sodium nitroprusside was administered to control the blood pressure when needed. Intraoperative hemodynamic changes resulting from the pneumoperitoneum and intraoperative manipulations were documented.

The surgical technique of transperitoneal laparoscopic adrenalectomy has been extensively described (2,5).

The follow-up of patients was done based on data review from medical records and telephone contacts. During the first year of follow-up, each patient was examined in at least four different occasions. Their blood pressure was measured and registered in their records. In the sixth and tenth months following the surgery, each patient was submitted to dosage of cathecholamines in urine and serum. They were submitted to MIBG at the end of the first year after surgery. After the first year, each patient was examined at least once a year and submitted to laboratory exams and MIBG for at least five years. All the cases included in the study had a minimum follow-up of 18 months (18 to 150 months, mean 74 months).

RESULTS

We successfully performed twenty-five laparoscopic adrenalectomies in twenty-four different patients. Twenty-three patients underwent unilateral LA and one patient underwent right total and left partial adrenalectomy for bilateral pheochromocytoma. This case was operated in two stages. Of the 25 interventions, 2 (8%) were converted to open surgery, one

Table 1 – Pre-operative data.

Case	Age (years)	Gender	Clinical Presentation	Antecedent	Side	CT - Tumor Size (mm)
1	52	Male	Hypertensive crises	None	Left	55
2	55	Female	Hypertension	Familial pheochromocytoma	Left	20
3	10	Male	Hypertensive crises	None	Right	30
4	38	Male	Hypertensive crises	Familial pheochromocytoma	Right	13
5	22	Male	Hypertensive crises	None	Right	10
6	42	Female	Hypertension	Hysterectomy	Left	15
7	46	Male	Hypertensive crises	None	Right	80
8	57	Male	Hypertension	Kidney transplantation	Left	10
9	65	Female	Incidentally discovered	Depression	Left	41
10	62	Male	Hypertension	Radical prostatectomy	Right	35
11	47	Male	Hypertensive crises	Cholecystectomy	Right	45
12	61	Male	Hypertensive crises	None	Right	15
13	41	Female	Hypertension	None	Left	20
14	15	Male	Abdominal pain Anxiety crises Without hypertension	None	Right	45
15	44	Male	Hypertensive crises	Medullary thyroid cancer Familial pheochromocytoma	Bilateral	40/25
16	40	Male	Hypertension	None	Right	60
17	45	Male	Hypertensive crises	None	Left	30
18	61	Female	Hypertensive crises	None	Right	30
19	41	Female	Hypertension	None	Right	50
20	47	Female	Hypertension	None	Right	40
21	54	Female	Incidentally discovered	Hysterectomy	Left	55
22	48	Male	Incidentally discovered	None	Right	5
23	75	Female	Incidentally discovered Hypertension	Bilateral lumbar sympathectomy	Left	120
24	36	Female	Incidentally discovered	None	Right	50

due to a major venous bleeding and the other due to difficulty in freeing the gland, located almost entirely behind the inferior vena cava.

The mean operative time, excluding the two converted cases, was 126 minutes (60 to 215 min.).

Intra-operative complications occurred in 4 (16.7%) patients (Table-2).

In one case, during specimen withdrawal, the extractor bag ruptured and the specimen was not found by laparoscopic inspection. It was necessary to make

a small incision in the abdomen to remove the gland. In another case, we had a small vena cava injury that was sutured by laparoscopy without any difficulty. A 10-year-old patient suffered an injury in anomalous right adrenal vein. The subsequent bleeding required conversion to open surgery. The oldest patient in this series, a 75-year-old woman with a 12 cm left adrenal tumor, there was an injury of the splenic artery during dissection. The arterial injury could not be repaired and a laparoscopic splenectomy was performed.

Table 2 – Intra-operative (IO) occurrences.

Case	IO Complication	Conduct	Operative Time (minutes)	Transfusion None	
1	Extractor bag rupture	Minilaparotomy	150		
2	None		135	None	
3	Venous injury	Conversion	Conversion	5 units IO	
4	None		140	None	
5	None		120	None	
6	None		80	None	
7	None		150	None	
8	None		70	None	
9	None		150	None	
10	Vena cava injury	Laparoscopic suture	215	None	
11	None	Conversion	Conversion	None	
12	None		75	None	
13	None		90/100 bilateral	None	
14	None		160	None	
15	None		150	None	
16	None		90	None	
17	None		75	None	
18	None		125	None	
19	None		60	None	
20	None		90	None	
21	None		120	None	
22	None		190	None	
23	Splenic artery injury	Laparoscopic splenectomy	180	2 units PO	
24	None		190	None	

PO = postoperative

No cases of severe hemodynamic instability were observed throughout the duration of anesthesia, but most of the patients had transient elevation of blood pressure during the manipulation of the gland, before adrenal vein ligation. These elevations were in general controlled with sodium nitroprusside.

Two (8.3%) patients had postoperative complications (Table-2). In one of the converted procedures, the patient developed an acute renal failure, postoperative ileum and subcutaneous infection. He left the hospital in a good condition on the 7th postoperative day. Another patient developed an abdominal and lumbar ecchymosis after hospital discharge with spontaneous resolution.

Two patients (8.3%) received a blood transfusion (Table-2), one of them in the operating room and the other during the first postoperative day.

All patients resumed oral nutrition and ambulation 1 to 2 days after the surgery.

The mean postoperative hospital stay was 3.8 days (1 to 11 days).

All the tumors were pathologically identified as pheochromocytomas. There was no evidence of malignancy such as local invasion or metastasis. The largest specimen removed measured 12 cm and weighed 200g (case 23).

Of the twenty patients who had symptomatic hypertension, 18 (90%) returned to normal blood

Table 3 – Postoperative (PO) results.

Case	PO Complication	Long-term Follow-up	Follow-up (months)	Final Diagnosis
1	None	Cure	150	Pheochromocytoma
2	None	Cure	144	Familial pheochromocytoma
3	None	Cure	43	Pheochromocytoma
4	None	Cure	140	Familial pheochromocytoma
5	None	Hypertensive crises	118	Pheochromocytoma
6	None	Cure	100	Pheochromocytoma
7	None	Cure	116	Pheochromocytoma
8	None	Cure	111	Pheochromocytoma
9	None	Cure	110	Non-secretory pheo
10	None	Cure	58	Pheochromocytoma
11	Renal failure, post-operative ileum, SC infection	Cure	108	Pheochromocytoma
12	None	Cure	19	Pheochromocytoma
13	None	Mild hypertension	87	Pheochromocytoma
14	None	Cure	84	Pheochromocytoma
15	None	Cure (death due to a heart attack after 18 months)	18	Familial pheochromocytoma
16	None	Cure	19	Pheochromocytoma
17	None	Cure	61	Pheochromocytoma
18	None	Cure	63	Pheochromocytoma
19	None	Cure	63	Pheochromocytoma
20	None	Cure	56	Dopamine-secretory pheo
21	None	Cure	18	Pheochromocytoma
22	None	Cure	48	Pheochromocytoma
23	None	Cure	24	Pheochromocytoma
24	Ecchymosis	Cure	18	Non-secretory pheo

pressure immediately after the surgery, during the hospital stay. In one of the patients the blood pressure level remained unchanged (hypertensive crises). Another patient persisted with mild hypertension, controlled with a single antihypertensive drug. These results remained unchanged during the follow-up.

In one of four normotensive patients, the blood pressure had a peak during the anesthetic induction but was easily controlled with sodium nitroprusside. Another normotensive patient complained of abdominal pain and anxiety. His symptoms

disappeared after surgery (case 14). All these 4 cases remained normotensive in the late postoperative period (Table-3).

During a mean follow-up of 74 months, no tumor recurrence or metastasis was observed.

One patient died 18 months after surgery because of myocardial infarction. This patient underwent bilateral surgery, with right total and left partial adrenal ectomy. He became normotensive and the postoperative adrenal function remained normal, without the use of glucocorticoids or mineralocorticoids (case 15).

COMMENTS

Since the first report of laparoscopic adrenalectomy by Gagner et al. in 1992, this procedure has become the preferred surgical management of benign adrenal tumors due to its numerous advantages (6). Comparative studies between open and laparoscopic surgery have shown that laparoscopic intervention should be considered the gold-standard procedure for adrenal surgery (7,8).

To date no relevant prospective and randomized series comparing laparoscopic adrenalectomy versus conventional surgery for pheochromocytoma, to our knowledge, has been published in the literature. Nevertheless, the accumulated international experience is significant and suggests that laparoscopic approach is better than open surgery regarding morbidity, bleeding, length of hospitalization, convalescence, postoperative pain and aesthetic sequels (7-9).

Pheochromocytoma was initially considered a contraindication to LA because it was reported by Meurisse et al. that pneumoperitoneum could promote an acute release of catecholamines (10). However, several authors have shown that when there is an adequate preoperative preparation these changes are discrete and well-tolerated by patients (11-13).

In a recent study, Sood et al. showed that the maintenance of a lower intraabdominal pressure (8-10 mmHg) reduces the release of catecholamines and helps prevent hemodynamic instability (14).

There are four possible laparoscopic approaches to the adrenal gland, mainly transperitoneal, lateral retroperitoneal, posterior retroperitoneal and trans-thoracic trans-diaphragmatic (15,16). The transperitoneal access is often preferred by many surgeons because of its broader working space and familiar anatomy. Nonetheless, retroperitoneal laparoscopic adrenalectomy has gained popularity because it provides direct access to the adrenal gland and avoids bowel handling and potential intraaabdominal viscera injury. Rubinstein et al. published a randomized trial with 56 patients at the Cleveland Clinic, showing that operative parameters, perioperative morbidity and pathological characteristics of the intact extracted specimen were similar between both approaches (17). The choice of laparoscopic approach for adrenalectomy varies according to personal experience and preference of the laparoscopic surgeon.

In our experience, the small incidence of complications, the short convalescence period and the long-term satisfactory results, have enabled us to establish the laparoscopic adrenalectomy as the procedure of choice in pheochromocytoma management.

With the introduction of robotic surgery, adrenalectomy using robotic endoscopic surgical devices (Da Vinci system) has recently been proposed. Morino et al., published a prospective randomized trial with 20 patients, comparing the outcomes of robotic (RA) versus lateral transperitoneal laparoscopic procedures. This study showed that RA is associated with a longer operative time, increased cost and a higher morbidity when compared to lateral transperitoneal LA (18). However, further studies are needed to define the role of robotic-assisted adrenalectomy (19).

Perioperative management of patients with phaeochromocytoma requires detailed knowledge of the potential complications. Intraoperatively, hypertensive crisis and tachyarrhythmia may occur resulting from massive catecholamine release. Thus, in agreement with other authors we consider preoperative treatment with the alpha-antagonist phenoxybenzamine obligatory (20).

Most research published on laparoscopic adrenalectomy refer to tumors smaller than 6 cm without pre-operative characteristics suggesting malignancy. Despite some reports of surgeries performed in large tumors with identified malignancy potential in pre-operative assessment, these procedures should be left to academic centers with extensive experience in laparoscopic surgery of the adrenal gland.

CONCLUSIONS

Our results have confirmed that laparoscopic adrenal ectomy for pheochromocytoma is a safe and effective procedure, providing the benefits of a minimally invasive approach. In our experience, the initial positive results obtained in the treatment of 24 patients were confirmed after a median follow-up of 74 months.

CONFLICT OF INTEREST

None declared.

REFERENCES

- 1. Karagiannis A, Mikhailidis DP, Athyros VG, Harsoulis F: Pheochromocytoma: an update on genetics and management. Endocr Relat Cancer. 2007; 14: 935-56.
- Mittendorf EA, Evans DB, Lee JE, Perrier ND: Pheochromocytoma: advances in genetics, diagnosis, localization, and treatment. Hematol Oncol Clin North Am. 2007; 21: 509-25.
- 3. Castilho LN, Medeiros PJ: O tratamento laparoscópico do feocromocitoma. Rev Cienc Med. 2003; 12:63-7.
- Kasturi S, Kutikov A, Guzzo TJ, Smith AL, Wein AJ: Modern management of pheochromocytoma. Nat Clin Pract Urol. 2007; 4: 630-3.
- Castilho LN: Suprarrenalectomia. In: Castilho LN (ed.), Laparoscopia Urológica. Campinas, LPC Comunicações. 2000; pp. 365-77.
- Gagner M, Lacroix A, Bolté E: Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. N Engl J Med. 1992; 327: 1033.
- Castilho LN, Liang LS, Ferreira U, Fregonesi A, Saade RD, Netto Jr,NR: Cirurgia do tumor benigno de supra-renal por videolaparoscopia. J Bras Urol. 1996; 22:33-6.
- 8. Castilho LN, Medeiros PJ, Mitre AI, Dénes FT, Lucon AM, Arap S: Pheochromocytoma treated by laparoscopic surgery. Rev Hosp Clin Fac Med Sao Paulo. 2000; 55: 93-100.
- 9. Janetschek G, Altarac S, Finkenstedt G, Gasser R, Bartsch G: Technique and results of laparoscopic adrenalectomy. Eur Urol. 1996; 30: 475-9.
- 10. Meurisse M, Joris J, Hamoir E, Hubert B, Charlier C: Laparoscopic removal of pheochromocytoma. Why? When? and Who? (reflections on one case report). Surg Endosc. 1995; 9: 431-6.
- Fernández-Cruz L, Sáenz A, Taurá P, Sabater L, Astudillo E, Fontanals J: Helium and carbon dioxide pneumoperitoneum in patients with pheochromocytoma undergoing laparoscopic adrenalectomy. World J Surg. 1998; 22: 1250-5.
- 12. Chigot JP, Movschin M, el Bardissi M, Fercocq O, Paraskevas A: Comparative study between laparoscopic and conventional adrenalectomy for pheochromocytomas. Ann Chir. 1998; 52: 346-9.

- Col V, de Cannière L, Collard E, Michel L, Donckier J: Laparoscopic adrenalectomy for phaeochromocytoma: endocrinological and surgical aspects of a new therapeutic approach. Clin Endocrinol (Oxf). 1999; 50: 121-5.
- Sood J, Jayaraman L, Kumra VP, Chowbey PK: Laparoscopic approach to pheochromocytoma: is a lower intraabdominal pressure helpful? Anesth Analg. 2006; 102: 637-41.
- Gill IS: Laparoscopic Adrenal Surgery. In: 95th Annual Meeting, Atlanta; 2000. Laparoscopic Organ Ablative Urology – Postgraduate Course. Houston: AUA Office of Education; 2000. p.1-4.
- Subramaniam R, Pandit B, Sadhasivam S, Sridevi KB, Kaul HL: Retroperitoneoscopic excision of phaeochromocytoma--haemodynamic events, complications and outcome. Anaesth Intensive Care. 2000; 28: 49-53.
- 17. Rubinstein M, Gill IS, Aron M, Kilciler M, Meraney AM, Finelli A, et al.: Prospective, randomized comparison of transperitoneal versus retroperitoneal laparoscopic adrenalectomy. J Urol. 2005; 174: 442-5; discussion 445.
- 18. Morino M, Benincà G, Giraudo G, Del Genio GM, Rebecchi F, Garrone C: Robot-assisted vs laparoscopic adrenalectomy: a prospective randomized controlled trial. Surg Endosc. 2004; 18: 1742-6.
- 19. Brunaud L, Bresler L, Ayav A, Zarnegar R, Raphoz AL, Levan T, et al.: Robotic-assisted adrenalectomy: what advantages compared to lateral transperitoneal laparoscopic adrenalectomy? Am J Surg. 2008; 195: 433-8
- 20. Knüttgen D, Wappler F: Anaesthesia for patients with phaeochromocytoma specifics, potential complications and drug strategies. Anasthesiol Intensivmed Notfallmed Schmerzther. 2008; 43: 20-7.

Accepted after revision: September 1, 2008

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EDITORIAL COMMENT

Surgical cure of pheochromocytomas is a real challenge and must be considered a model when multidisciplinary approach is essential to achieve the best results. The endocrinologist, cardiologist, the anesthesiologist as well as the surgeon must work together to avoid the devastating effects of non programmatic surgical approach that in the past had high mortality (1).

Pheochromocytomas often secrete catecholamine that causes vasoconstriction and hypertension as the main symptom. The complications of the adequate treatment are mild, and mortality is more related to the patient's condition than to the surgical technique (2).

The variations on the blood pressure are the biggest problem during the anesthetic procedure. Endocrine and cardiologic preparations before the operation are the first steps to reduce complications. Alpha-blocking agents in the pre operative period are obligatory in the majority of patients for at least 15 days before the procedure. Beta blocking can be associated in cases of excessive tachycardia or arrhythmias. Fluid intake prior to the procedure is also mandatory (3). Echocardiogram defines selected patients with excessive compromises of left ventriculum when cardio tonics can show some benefits (4). After surgical resection, hypotension or left ventriculum failure may occur and vasopressors must be infused (3). Particularly when considering cure of hypertension after surgery, cardiac failure can be considered a confounding factor for the immediate evaluation.

As regards the surgical technique, in the past ten years laparoscopic surgery has become the gold standard for tumors smaller than 6 cm (5). At the beginning of the laparoscopic experience, it has been thought that pneumoperitoneum could affect the blood pressure during surgery (6).

Some contemporary reports have shown that the variation in blood pressure occurred independently conventional surgery or laparoscopic approach (7,8). Additionally, some authors have defended that beyond the vantages of lower bleeding and faster recovery, the delicate manipulation on laparoscopic technique would be an additional for minimum invasive procedure (8-11).

Into pheochromocytoma surgery, it is important to have an early stage control of the main adrenal vein with the intention of reducing the blood pressure decompensation, yet it has been a questionable paradigm these days (9). Some studies have proposed that the early control of the vein could be done only via the transperitoneal technique, Salomon et al. described the feasibility of doing this through extra peritoneal approach (10).

In our experience the control of the vein is not only bilateral feasibly but seems easier on the right side (where the adrenal vein is shorter and frequently retrocaval), than through transperitoneal approach, specially, when it is a large tumor (11).

Another important issue is the treatment of the malignant disease that occurs in approximately 10 % (12). Some initial series suggest that it is possible to offer laparoscopic treatment with good results, but there are some cases of tumor recurrence and portal implants (13).

The benefit of the laparoscopic procedure in the case of malignant pheochromocytoma at a locally confined stage still remains unclear and requires prospective, randomized studies.

REFERENCES

- Gagner M, Pomp A, Heniford BT, Pharand D, Lacroix A: Laparoscopic adrenalectomy: lessons learned from 100 consecutive procedures. Ann Surg. 1997; 226: 238-46; discussion 246-7.
- 2. Gil-Cárdenas A, Cordón C, Gamino R, Rull JA, Gómez-Pérez F, Pantoja JP, et al.: Laparoscopic adrenal-ectomy: lessons learned from an initial series of 100 patients. Surg Endosc. 2008; 22: 991-4.
- 3. Adams HA, Hempelmann G: Anesthesia for patients with pheochromocytoma. Our own results and a review. Anasthesiol Intensivmed Notfallmed Schmerzther. 1993; 28: 500-9.
- 4. Meune C, Bertherat J, Dousset B, Jude N, Bertagna X, Duboc D, et al.: Reduced myocardial contractility assessed by tissue Doppler echocardiography is associated with increased risk during adrenal surgery of patients with pheochromocytoma: report of a preliminary study. J Am Soc Echocardiogr. 2006; 19: 1466-70.

- 5. Guazzoni G, Cestari A, Montorsi F, Bellinzoni P, Centemero A, Naspro R, et al.: Laparoscopic treatment of adrenal diseases: 10 years on. BJU Int. 2004; 93: 221-7.
- 6. Mittendorf EA, Evans DB, Lee JE, Perrier ND: Pheochromocytoma: advances in genetics, diagnosis, localization, and treatment. Hematol Oncol Clin North Am. 2007; 21: 509-25.
- 7. Pugliese R, Boniardi M, Sansonna F, Maggioni D, De Carli S, Costanzi A, et al.: Outcomes of laparoscopic adrenalectomy. Clinical experience with 68 patients. Surg Oncol. 2008; 17: 49-57.
- Tobias-Machado M, Rincón Ríos F, Tulio Lasmar M, Tristão R, Hermínio Forseto P Jr, Vaz Juliano R, et al.: Laparoscopic retroperitoneal adrenalectomy as a minimally invasive option for the treatment of adrenal tumors. Arch Esp Urol. 2006; 59: 49-54.
- 9. Lang B, Fu B, OuYang JZ, Wang BJ, Zhang GX, Xu K, et al.: Retrospective comparison of retroperitoneoscopic versus open adrenal ectomy for pheochromocytoma. J Urol. 2008; 179: 57-60; discussion 60.

- Salomon L, Rabii R, Soulie M, Mouly P, Hoznek A, Cicco A, et al.: Experience with retroperitoneal laparoscopic adrenalectomy for pheochromocytoma. J Urol. 2001; 165: 1871-4.
- 11. Tobias-Machado M, Lasmar MT, Zambon JP, Tristão R, Forseto PH Jr, Juliano RV, et al.: Laparoscopic adrenalectomy: a prospective study comparing transperitoneal and retroperitoneal approaches. Rev Assoc Med Bras. 2006; 52: 208-13.
- 12. Strong VE, Kennedy T, Al-Ahmadie H, Tang L, Coleman J, Fong Y, et al.: Prognostic indicators of malignancy in adrenal pheochromocytomas: clinical, histopathologic, and cell cycle/apoptosis gene expression analysis. Surgery. 2008; 143: 759-68.
- 13. Tobias-Machado M, Tristão RA, Silva MNR, Wroclawski ER: Laparoscopic adrenalectomy for malignant disease: Technical feasibility and oncological results. Einstein. 2007; 5: 44-47.

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EDITORIAL COMMENT

The surgical management of patients with pheochromocytoma is potentially curative and it has always been a question of debate because of the clinical complexity of such patients with potential high-risk peri-operative morbid-mortality.

When laparoscopic surgery was introduced as an alternative approach for open surgery the tension rose among traditional surgeons, used to the common problems associated with patients with pheochromocytoma, that were mainly concerned with the safety of the laparoscopic approach.

As the experience among laparoscopists grew, it became clear that this approach was not only a matter of better cosmesis, whereas on the contrary, several reports revealed the benefits of treating patients with pheochromocytoma preferentially via laparoscopy

over the conventional open approach, such as less cathecolamines release (1), less bleeding (1,2), less UCI length of stay (2), less hospital stay (1,2), shorter convalescence (1) and mainly revealing to be as safe as open surgery (1,2).

Castilho and colleagues, in this issue of the Int Braz J Urol reported on the long-term follow-up of 24 patients who underwent laparoscopic adrenalectomy for pheochromocytoma over an 11-year period with a mean follow up of 74 months. Castilho's study found that only one patient was not totally cured in the period studied (1 out of 24 - 4.2%); this single patient continued to have an hypertensive crisis and another patient continued with mild hypertension under control. No tumor recurrence was observed. The Castilho et al. report is very important to demonstrate the long-term

safety of laparoscopic approach as a means of cure and tumor recurrence, in addition to the safety also reported during the peri-operative time.

Treatment of patients with pheochromocytoma requires a committed multidisciplinary team of urologist, endocrinologist, anesthesiologist, radiologist and all staff in a well equipped hospital and aware of all potential needs of such patients. Laparoscopic surgery performed by an experienced surgical group along a knowledgeable committed multidisciplinary team in a prepared hospital have proven efficacy and safety. It should be kept in mind that laparoscopy is only one of the advances now applied to patients with pheochromocytoma.

Nevertheless, laparoscopic surgery may not yet have eliminated open surgery. At our institution, 4 patients with pheochromocytoma out of 51 (8%) that

were operated on from 2000 to 2008 (non-published data) still required open conventional approach either because of major vessel involvement or tumor size greater than 10 cm or adjacent organ concomitant removal.

Further studies are encouraged to continue to improve our surgical results on such complex patients with a complex disease.

REFERENCES

- 1. Gill IS: The case for laparoscopic adrenalectomy. J Urol. 2001; 166: 429-36.
- Faria EF, Andreoni C, Krebs RK, Nascimento H, Goldman SM, Kater C, et al.: Advances in pheochromocytoma management in the era of laparoscopy. J Endourol. 2007; 21: 1303-7.

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EDITORIAL COMMENT

Pheochromocytomas are relatively uncommon tumors whose operative resection has clear medical and technical challenges.

While the safety and efficacy of laparoscopic adrenalectomy are relatively well documented, few studies with extended follow-up have been conducted to measure the success of the procedure for the most challenging of the adrenal tumors. In addition, several reports have questioned the applicability of a minimally invasive approach for pheochromocytomas larger than 6 cm in diameter. This paper from Castilho et al. evaluated long term results of laparoscopic adrenalectomy in patients with pheochromocytoma (diameter ranging from 10 to 120 mm) and authors have to be commended for this interesting work. As other series of laparoscopic resection for pheochromocytoma, this paper shows that despite appropriate perioperative medical management, intraoperative hypertensive remains a valid concern especially during intra-abdominal insufflation and tumor manipulation (1). In

addition, it emphasizes that laparoscopic approach to these tumors has traditionally been associated with higher complication rates than adrenalectomy for other indications. Lesions larger than 6 cm are associated with longer operative times and may be more difficult to safely resect laparoscopically. Extreme care must be taken to avoid intraoperative capsular disruptions and lifetime follow-up is an important aspect of the postoperative care of the pheochromocytoma patient (1). Recently, robotic technology has been introduced providing a 3-dimensional display that enhances depth perception, enabling the surgeon to operate in a comfortable seated position in which the eye, hand, and target are in line, and the instruments contain a "wrist" joint to improve dexterity. These advantages could theoretically improve laparoscopic adrenalectomy procedure and then subsequently lead to improved perioperative and postoperative outcomes. We recently reported 24 patients with pheochromocytoma who underwent unilateral robotic-assisted

adrenalectomy (2). Conversion rate was 8.3% and tumor capsule was ruptured in 1 patient with a right 7.5 cm cystic pheochromocytoma (cyst rupture).

Moreover, per-operative hemodynamic modifications seem to be similar during robotic and conventional adrenalectomy for pheochromocytoma (unpublished data). This emphasizes that robotic approach can not be considered de facto as precluding all difficulties that can be observed during conventional laparoscopic adrenalectomy for pheochromocytoma. Laparoscopic excisions of pheochromocytomas with or without robotic system remain challenging surgical procedures because of intraoperative catecholamine release and tumor vascularization. Extensive experience in minimally invasive techniques, as well as in endocrine surgery are two key elements for surgeons performing laparoscopic adrenalectomy for pheochromocytoma.

REFERENCES

- 1. Kercher KW, Novitsky YW, Park A, Matthews BD, Litwin DE, Heniford BT: Laparoscopic curative resection of pheochromocytomas. Ann Surg. 2005; 241: 919-26; discussion 926-8.
- 2. Brunaud L, Ayav A, Zarnegar R, Rouers A, Klein M, Boissel P, Bresler L: Prospective evaluation of 100 robotic-assisted unilateral adrenalectomies. Surgery. 2008; 144: 995-1001.

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