Laparoscopic adrenalectomy in pheochromocytomas

M. Guerrieri[1], M. Baldarelli[1], M. Scarpelli[2], S. Santini[1], G. Lezoche[3], and E. Lezoche[3]

[1]Department of General Surgery; [2]Department of Pathological Anatomy, University of Ancona, Ancona; [3]Department of General Surgery, University "La Sapienza", Policlinico "Umberto I", Roma, Italy

ABSTRACT. ***Background:*** **The aim of this study was to evaluate 17 patients undergoing laparoscopic adrenalectomy for the treatment of pheochromocytoma by transperitoneal anterior approach.** ***Methods:*** **Seventeen patients underwent laparoscopic adrenalectomy for pheochromocytoma between January 1994 and May 2002. Ten females (58.8%) and 7 males (41.2%) were operated on; 14 patients (82.3%) had sporadic pheochromocytoma and 3 (17.7%) were familiar cases. Mean age was 42 yr (range 25-72 yr). All patients were treated pre-operatively with α-blockers. Seven patients (41.2%) underwent right adrenalectomy; 9 (52.9%) underwent left adrenalectomy and 1 (5.9%) bilateral adrenalectomy.** ***Results:*** **No conversion to open surgery occurred and no mortality was observed. The right-side adrenalectomy required a mean operative time of 86 min (range 45-120), the left-side procedure a mean operative time of 116 min (range 80-140) and the bilateral one 219 min. In two patients (11.8%), a laparoscopic cholecystectomy and ovariectomy, respectively, were performed without changing the position of the patient on the operating table. Only 1 patient (5.9%) presented significant intraoperative hypertension, and arrhythmia resolved by medical therapy. No other intraoperative and post-operative complications were reported. Mean hospital stay was 3 days (range 2-8 days). At mean follow-up of 48 months (range 6-96 months), regression of symptoms and control of blood pressure were obtained without additional treatment in all patients. No recurrences were reported.** ***Conclusion:*** **In our experience, adrenal pheochromocytoma can be treated safely and effectively by laparoscopic transperitoneal anterior approach.**

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INTRODUCTION

Surgical approach to adrenal gland had always aroused controversies among surgeons for its deep, retroperitoneal location and the complexity of the pathologies, as is the case of pheochromocytoma. Surgical access is difficult and associated with high morbidity and long convalescence.

In 1992, Michel Gagner described the first laparoscopic transperitoneal adrenalectomy with the patient in a lateral decubitus position (1). This initial report has been followed by several ones using the same approach or, as an alternative, the transperitoneal approach with the patient supine or the retroperitoneal approach with the patient in the prone or in the lateral decubitus position (2-6).

The data in the literature have largely confirmed the safety and efficacy of these techniques, so that minimally invasive adrenalectomy can actually be considered the treatment of choice for a variety of benign lesions and also for lesions involving the medulla (7-13).

The aim of this paper is to report a retrospective analysis of data concerning 17 patients who underwent laparoscopic adrenalectomy with a transabdominal anterior approach for the treatment of pheochromocytoma, and to evaluate the relationship with the possible risk of cardiovascular complications as well as the technical difficulties in case of large size tumors.

MATERIALS AND METHODS

Patients

From January 1994 to January 2002, 162 laparoscopic adrenalectomies were performed in 2 different centres (Department of General Surgery of the University of Ancona and Department of Surgery "Paride Stefanini" of the University "La Sapienza" in Roma) using the transperitoneal anterior approach. All patients were subjected to a baseline hormonal test including diurnal rhythm of plasma cortisol, urinary free cortisol (UFC), ACTH, DHEAS, 17-OHProgesterone (17-OHP), testosterone, supine and upright plasma renin activity (PRA) as well as al-

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Correspondence: M. Guerrieri, Dipartimento di Chirurgia generale, Università di Ancona, Via Flaminia 393, 60020 Palombina Nuova, Ancona, Italy.

E-mail: guerrieri.m@libero.it

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dosterone, urinary aldosterone, catecholamines excretion and vanillin mandelic acid (VMA). Computerized tomography (CT) and magnetic resonance imaging (MRI) were performed in all patients. Of the 162 patients, 23 were admitted with the clinical, imaging and laboratory features of presumed pheochromocytoma. All these patients underwent Se75-cholesterol or ^{131}I-metaiodobenzylguanidine (^{131}I-MIBG) radioisotopic scintigraphy. The pre-operative diagnosis of pheochromocytoma was histologically demonstrated in 17 patients and only these were included in the present study. Eighteen laparoscopic adrenalectomies were performed by transperitoneal anterior approach in 17 patients: 7 right adrenalectomies (38.8%), 9 left (50%) and only 1 bilateral (11.1%). The group of patients included 10 women (58.8%) and 7 men (41.2%) with mean age of 42 yr (range 25-72 yr). Out of the 17 patients with pheochromocytoma, 14 (82.4%) were found to be sporadic and 3 (17.6%) were patients with familial inheritance.

The hereditary cases were clinically relevant. One of them was a patient with Von Recklinghausen disease (fibromatosis), who underwent right adrenalectomy after being subjected to left adrenalectomy elsewhere 7 yr before. The two other patients presented with a particular clinical feature, being brother and sister affected by MEN2A syndrome (mutation of the protocongen RET, exon11, codon634) and both operated for thyroidectomy for medullary carcinoma and then adrenalectomy. The brother was the only case of bilateral adrenalectomy for pheochromocytoma performed.

As for the symptoms of the disease, 4 patients (23.5%) had occasional symptoms, 6 patients (35.3%) presented with classical hypertensive paroxysmal crises in a normotensive clinical feature, 4 subjects (23.5%) presented with basic hypertension associated with paroxysmal crises and 2 (11.7%) were only hypertensive. One of these had epigastric pain during the hypertensive crises. One patient (5.9%) with MEN2A presented with anxiety-depression symptoms which resisted pharmacologic therapy. Pharmacologic therapy (doxazosin 4 mg/day) was administered to all patients to lower the pressure levels ten days before the operation. The mean pre-operative blood pressure was 95 mmHg (range 90-100 mmHg) for diastolic pressure and 145 mmHg (range 140-160 mmHg) for systolic pressure. According to our protocol, blood pressure was continually monitored and recorded before and during the anesthesia.

An intraoperative ultrasound study of contralateral gland was carried out in 4 patients (23.5%) where a bilateral pheochromocytoma or a ganglia localization were pre-operatively suspected.

All patients were regularly followed-up by control of blood pressure and plasma concentration of catecholamines every 6 months for the first 2 yr and every 1 yr thereafter. Hereditary cases were also subjected to ^{131}I-MIBG scintigraphy.

Surgical techinique

In each case, laparoscopic adrenalectomy is performed using the transperitoneal anterior approach with the patient in the supine position. The table is rotated about 30° degrees bringing up the side of the patient where the lesion is located. The video screen is placed at the head of the table, homolateral to the lesion to be removed. The surgeon is standing on the ipsilateral side of the lesion. The operation begins with the creation of pneumoperitoneum at a pressure of 14 mmHg with a Veress needle or, as an alternative, with an open technique and Hasson cannula if the presence of adhesions from previous operations is suspected. In every case, 4 trocars and a 45° laparoscope are employed in order to have a better vision in a restricted space.

Right adrenalectomy

The first 12 mm trocar is placed in a right paramedian position, two fingerbreadths below the costal arch. Two more 12 mm trocars are placed, one along the right midclavicular line 4 cm above the transverse umbilical line, and one along the middle or posterior axillary line at the level of the umbilicus. The latter trocar is placed in the peritoneal cavity under vision in the lateral most position, which may correspond to the middle or the posterior axillary line according to the patient's anatomy. In any case, the kidney is not in the way of the instruments introduced through this trocar. The fourth trocar is placed below the xyphoid process to the left of the midline. After exploring the peritoneal cavity, the table is tilted to an anti-Trendelemburg position and to the left (right side up), to facilitate exposure of the surgical field. Any adhesion between the gallbladder and the omentum or the transverse colon is taken down so as to expose Morrison's pouch by raising the liver with a retractor (Auto Suture Endo Retract II, United States Surgical Corporation, Norwalk, Connecticut, USA) introduced from the subxyphoid trocar. The posterior peritoneum is then divided along the right margin of the inferior vena cava, prolonging the peritoneal incision towards the diaphragm, where the adrenal gland tissue is easily recognized from the retroperitoeal subdiaphragmatic fatty tissue by its typical yellow ochre colour. The middle adrenal vein is identified by blunt dissection, without any instrumental manipulation of the gland itself to avoid spillage of neoplastic cells. The vein is thus isolated and closed with 8 mm curved titanium clips (Ligaclip, Ethicon Endo-Surgery, INC, Cincinnati, Ohio, USA), placing two clips on the vena cava side and one clip on the adrenal side. Once the main vein is closed, the dissection proceeds more rapidly, first by isolating the retrocaval portion of the adrenal gland, then by dividing the small subdiaphragmatic arterial branches and then by separating the adrenal gland from the kidney. The specimen is introduced into a specimen retrieval bag (EndoCATCH, 10 mm Autosuture Company, USSC Norwalk Connecticut, USA) and removed from the peritoneal cavity through the most lateral trocar. The incision is enlarged in relation to the size of the lesion.

Care is taken during the entire procedure to avoid any manipulation of the gland with preventive ligature of the main adrenal gland for the possible spillage of catecholamines.

Left adrenalectomy

Trocar position for left adrenalectomy mirrors trocar position for the right side. The procedure begins by dividing the peritoneum along the left parieto-colic gutter and prolonging the peritoneal incision towards the sigmoid colon. After dividing the splenocolic ligament, the left colon is mobilized by blunt dissection and reflected off Gerota's fascia. Once the inferior margin of the pancreatic tail has been identified, Gerota's fascia is divided to expose the adrenal gland which is recognized by its typical yellow color. The left adrenal vein is identified running in a caudal direction towards its confluence with the left renal vein and it is divided between curved titanium clips. Again, one should refrain from any direct manipulation of the gland during dissection to avoid spillage of catecholamine. The specimen is removed from the peritoneal cavity inside a specimen retrieval bag.

RESULTS

No conversion to open surgery and no mortality were reported. Anterior transperitoneal laparoscopic adrenalectomy was feasible in all patients with clinical indications of pheochromocytoma. Mean operative time for right and left adrenalectomy were 86 (range 45-120 min) and 116 min (range 80-140 min), respectively; bilateral adrenalectomy required 219 min. In two patients (11.8%), one cholecystectomy and one ovariectomy, respectively, were performed without additional trocars and without changing the patient's position on the surgical table. No other localizations were found in 4 patients (23.5%) who underwent intraoperative contralateral ultrasound exploration. The intraoperative course was uneventful in 16 patients (94.1%). Only one patient (5.9%) presented significant intraoperative hypertension and arrhythmia easily controlled pharmacologically without sequelae. In the other patients, ns modifications of the blood pressure were recorded.

No intra- or post-operative blood transfusions were required. Mean blood loss was 150 ml (range 50-350 ml). All patients were ambulating freely and tolerating a light diet within 24 h after surgery. Post-operative pain was minimal and only 4 patients (23.5%) required the administration of a single dose of analgesic (ketorolac 30 mg).

Mean hospital stay was 3 days (range 2-8 days). Mean size of pheochromocytoma was 6.5 cm (range 3-10 cm), and the average weight of the gland was 40.5 g (range 13-145 g).

Mean follow-up was 48 months (range 6-96 months). Long-term follow-up results were excellent: all patients presented normalization of blood pressure values and none of them needed pharmacological therapy. No recurrences were reported. In hereditary cases, the ^{131}I-MIBG scintigraphy was negative for recurrence. Two patients (11.8%) died of another disease after 2 and 3 yr, respectively, after the operation.

DISCUSSION

Surgical excision represents the only successful therapy for pheochromocytoma. The aim of this study was to evaluate the results of laparoscopic adrenalectomy with transperitoneal anterior approach for the treatment of pheochromocytoma. Our hypothesis was that transperitoneal approach with the patient supine would be more rational for the treatment of adrenal pheochromocytoma, in order to reduce the risk of spread of catecholamines from adrenal gland.

The treatment of pheochromocytoma is still a delicate, complex procedure and, in our opinion, should be performed only in departments with a well established, multidisciplinary experience in adrenal gland pathology.

In fact, surgery for pheochromocytoma is accompanied by risk of hypotensive or hypertensive crisis due to excessive catecholamine excretion, which cannot be completely prevented by adequate pre-operative treatment with α-blockers (12).

The purpose of medical treatment is not the reduction of hormonal secretion but the prevention of the peripheral effects of catecholamines secreted by the tumor, so that the patient may undergo surgery with the best cardiovascular conditions (14).

Advances in pre-operative monitoring and the introduction of pre-operative blocking of α1 receptors have radically reduced the mortality rate (15).

Despite a significant increase in the rates of plasma norepinephrine related to peritoneal insufflation and mobilisation (15) of the adrenal gland, the adrenalectomies were performed with a low rate of morbidity as reported by several other reports (16-18).

One study (12) has demonstrated that severe hypertension was triggered only by direct manipulation of the adrenal gland but not by the pneumoperitoneum. For this reason, we still consider the early clipping of the main adrenal vein as mandatory, together with the avoidance of any manipulation of the gland (17).

The choice of the best laparoscopic approach to the adrenal gland in case of pheochromocytoma is still debated. If we look at open surgery, the posterior retroperitoneal approach is preferred in order to reduce the risks of a wide abdominal incision with possible post-operative complications (wound infection, incisional hernia) and those related to bowel manipulation (post-operative ileus, etc.) (1, 5).

In a previous work, we have demonstrated that the retroperitoneal posterior approach can be of choice in case of small adrenal masses, in obese patients and in patients with previous abdominal operations (17). Nevertheless, this approach entails risks due to a number of considerations: a) in case of bleeding, the patient's position is unfavourable for rapid conversion; b) the position does not make it possible to perform associated surgical procedures; c) particularly for pheochromocytoma, we must take into account the impossibility to explore the contralateral gland without changing the patient's position; d) the position of the patient on the operating table can impair or make the hemodynamic conditions worse.

Following the transperitoneal lateral approach, that is the most widely adopted thanks to Michel Gagner who first used it (1, 4), the access to both the kidney and the adrenal gland is obtained *via* the flank. This approach makes it possible to obtain the following advantages: a) rapid access to the gland with minimal trauma for the patient; b) the gravity aids in keeping bowels and blood away from the operating field; c) less wide dissection on the left side.

If we look at the disadvantages of this approach, the operative field is less large than the one provided by the anterior access, and no associated surgical procedures can be performed without changing the patient's position on the operating table. Moreover, this approach also doesn't allow the exploration of the contralateral gland to perform the bilateral excision without the patient's reposition. In the flank approach, as reported by Gagner, the first step, mostly for the left adrenalectomy, is the dissection of the lateral and anterior part of the adrenal gland and the adrenal vein can be identified early during the dissection only in case of smaller adrenal lesions.
On the contrary, when adopting the anterior approach, we achieve an early control of the adrenal vein without a significant manipulation of the gland. In fact, the anterior transperitoneal approach allows the identification and the ligature of the adrenal vein before reaching the area where the gland is located. The only disadvantages that we can observe with transperitoneal anterior approach are the wider dissection on the left side and the longer operating time.
Following this surgical strategy, only in one case did we observe a significant intraoperative change of the blood pressure, easily controlled medically: in the remaining 16 patients, the blood pressure was within the normal range and did not require any significant intraoperative pharmacological treatments. If we compare these results to our previous open surgery experience (unpublished data), we can conclude that the anterior laparoscopic procedure for pheochromocytoma is safe. Thanks to the transperitoneal anterior approach, associated cholecystectomy and ovariectomy could be performed without positioning any additional trocars and without changing the patient's position on the operating table. As for the associated procedures, the total operative time was 160 min, a short time only permitted by the anterior approach. An additional advantage of anterior access is the opportunity to perform an intraoperative ultrasound evaluation of the contralateral gland and in our experience this further investigation was performed in 4 patients where a bilateral pheochromocytoma or a ganglia involvement were pre-operatively suspected (19). Finally, adopting the anterior position bilateral adrenalectomy was performed, which was made possible by the simple rotation of the operating table.
In 1999, at the World Congress of Endoscopy held in Vienna, we presented a study showing that the size of the lesion, up to 10 cm of diameter, did not affect the outcome of the laparoscopic approach nor the operative time. This observation has been confirmed by Kazaryan's recent study (20), that reported results in agreement with our work. In our experience, the intraoperative blood loss was not correlated with the tumor size. Hospitalization was quite short. This prevented the development of classical complications (bronchopneumonic infections or deep venous thrombosis of the lower limbs) due to bed confinement.
In all the patients, the clinical symptoms and hypertension disappeared immediately after the operation without the need of any pharmacological therapy. A mean 4-yr follow-up has shown no local recurrences.
In conclusion, our data are in agreement with works from other groups showing the feasibility of laparoscopic adrenalectomy for pheochromocytoma. Following adequate pre-operative α blockade, good hemodynamic stability could be maintained during surgery. Our experience has shown that the specific surgical risks for pheochromocytoma are not enhanced by the laparoscopic approach. Thus, we can extend the benefits of minimally invasive surgery to the patients with pheochromocytoma who may gain advantage from a less invasive procedure, as compared to an open operation, with a shorter recovery time. The laparoscopic transabdominal anterior access with the patient supine allows an early ligation of the main adrenal vein before any further manipulation of the adrenal gland, which is of crucial importance in the management of pheochromocytoma. Finally, this approach does not require a change in the patient's position, neither in case of bilateral adrenalectomy nor for conversion when this is required.

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