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Laparoscopic transperitoneal anterior adrenalectomy in pheochromocytoma: experience in 62 patients

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Abstract
Background Aim was to evaluate the results in 62 patients undergoing laparoscopic adrenalectomy (LA) for the treatment of pheochromocytoma (PHE), with a transperitoneal anterior approach for lesions on the right side, and with a transperitoneal anterior submesocolic approach in case of left-sided lesions.
Methods Sixty-two patients underwent LA for the treatment of PHE at two centers in Rome and Ancona (Italy). Two patients had bilateral lesions, for a total of 64 adrenalectomies. Sporadic PHE occurred in 57 patients (91.9 %) and in 5 (8.0 %) it was familiar. Thirty-six patients (58.0 %) underwent right adrenalectomy, 24 (38.7 %) left adrenalectomy, and in 2 cases (3.2 %) LA was bilateral. In 38 cases of right adrenalectomy (59.3 %) and in 5 cases of left adrenalectomy (7.8 %), the approach was a transperitoneal anterior one. A transperitoneal anterior submesocolic approach was used in 21 left adrenalectomy cases (32.8 %).
Results Mean operative time for right and left transperitoneal anterior LA was 101 min (range 50–240) and 163 min (range 50–190), respectively. Mean operative time for left transperitoneal anterior submesocolic LA was 92 min (range 50–195). For bilateral adrenalectomy, mean operative time was 210 min (range 200–220). Conversion to open surgery occurred in 2 cases (3.22 %) due to extensive adhesions (1) and hemorrhage (1). One major and three minor complications were observed. Mobilization occurred on the first postoperative day. Hospitalization was 4.8 days (range 2–19). The lesions had a mean diameter of 4.5 cm (range 0.5–10).
Conclusions Early identification with no gland manipulation prior to closure of the adrenal vein is the main advantages of the transperitoneal anterior approach. PHE may be treated safely and effectively by a laparoscopic transperitoneal anterior approach for right-sided lesions and with a transperitoneal anterior submesocolic approach for left-sided ones.

Keywords Adrenal tumors · Laparoscopic adrenalectomy · Pheochromocytoma · Transperitoneal anterior approach

The surgical approach to the adrenal gland has raised debate among surgeons due to its deep, retroperitoneal location and for complexity in the management of secreting tumors, particularly in case of pheochromocytoma (PHE). The open approach requires a wide abdominal wall incision and is associated with higher morbidity rate and longer postoperative stay [1–3]. In 1992, Gagner described the laparoscopic transperitoneal approach with the patient in lateral decubitus position for adrenalectomy [4]. This initial experience has been followed by others using the same approach or, alternatively, the transperitoneal approach with the patient supine, the retroperitoneal approach with the patient in the prone, or in the lateral decubitus position [5–7]. Several reports have confirmed the safety and

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efficacy of these techniques, and minimally invasive adrenalectomy is presently considered the treatment of choice for a variety of benign lesions, including lesions of the medulla [8–10]. Aim of this study is to report the results of a retrospective analysis of prospectively collected data in 62 patients who underwent laparoscopic adrenalectomy (LA) with a transperitoneal anterior approach for the treatment of PHE, and to evaluate the relationship with the risk of cardiovascular accidents as well as the technical difficulties in case of large sized tumors.

Materials and methods

From January 1994 to December 2012, 62 patients underwent LA in two centers (Department of General Surgery, Surgical Specialties and Organ Transplantation, "Paride Stefanini," "Sapienza" University of Rome and Department of General Surgery, Università Politecnica delle Marche, Ancona, Italy) who follow the same protocol and use an identical transperitoneal anterior approach to adrenal gland lesions. Two patients had bilateral lesions, for a total of 64 laparoscopic adrenalectomies. Preoperative evaluation included history, physical examination, and laboratory tests such as plasma Cortisol, urinary free Cortisol, ACTH, DHEAS, 17-OHProgesterone, testosterone, supine and upright plasma renin activity, as well as aldosterone, urinary aldosterone, catecholamines' excretion, and vanillylmandelic acid evaluations. All patients underwent computerized tomography and magnetic resonance imaging before surgery and were admitted with a preoperative diagnosis of PHE. All patients underwent preoperative pharmacological preparation with alpha-blockers (doxazosin 20 mg/day), starting at least 15 days before surgery, as recommended [11–14]. If patients reported episodes of tachycardia, beta-blockers were also administered (atenolol 100–200 mg/day orally). On the day before surgery, treatment with alpha-blockers was discontinued, and normal saline 2,000 cc was administered i.v.to expand the plasma volume, in accordance with the endocrinologist's and anesthesiologist's consultation [14]. The lesions were located on the right in 36 (58.06 %), on the left in 24 (38.70 %), and were bilateral in 2 (3.22 %) (35 women, 27 men, mean age 51 years, age range 25–84 years) cases. A transperitoneal anterior approach was used in 38 cases of right adrenalectomy (59.37 %) and in 5 cases of left adrenalectomy (7.81 %). A transperitoneal anterior submesocolic approach was used in 21 left adrenalectomy cases (32.81 %). Out of 62 patients, PHE was sporadic in 57 (91.93 %) and familial in 5 (8.06 %). Of these, two were within a Von Recklinghausen's disease (fibromatosis) and three had a MEN 2A syndrome. Of the three patients with MEN 2A syndrome, one underwent bilateral adrenalectomy and the other two had previously undergone thyroidectomy for medullary carcinoma. Blood pressure and heart rate were continuously monitored and recorded before, during, and after anesthesia. If pressure increases were observed, clonidine or nitroglycerin was administered. Technical difficulties were evaluated on the basis of conversion rate and procedure duration.

Surgical techniques

Surgery is performed under general anesthesia. A nasogastric tube and urinary catheter are positioned. Intraoperative patients' monitoring includes intra-arterial radial artery catheter for continuous blood pressure measurement and a central venous catheter (subclavian or internal jugular access) for rapid infusion of liquids should be required. Pneumoperitoneum is usually established with a Veress needle at the umbilicus, or with an open technique and Hasson cannula, in case of the presence of abdominal scars from previous surgery. Pneumoperitoneum is set at a pressure of 12–13 mmHg, with carbon dioxide flow adjusted at 30 l/min. Four trocars and a 30°/45° forward oblique optic are used. This approach is performed with the patient supine, in slight anti-Trendelemburg position and with the operating table turned 30° with the side opposite the lesion down, to facilitate exposure of the surgical field. The surgeon stands on the side which is ipsilateral to the lesion.

The techniques for right and left anterior adrenalectomy have been previously described in detail [15–17].

Left adrenalectomy: transperitoneal anterior submesocolic approach

This approach is alternative to the anterior transperitoneal one with left colonic flexure mobilization which has been previously described, but with the same trocars' position (Fig. 1). The optic is introduced from trocar n. 3, while trocars 1 and 4 are the operating ones. Again, with the operating table in slight anti-Trendelemburg position and a lateral tilt with left side up, the transverse mesocolon is raised by the assistant with atraumatic forceps introduced from trocar n. 2, to expose the first jejunal loop at the ligament of Treitz and to identify the inferior mesenteric vein. The posterior peritoneum is opened at the insertion of the transverse mesocolon to the lower edge of the pancreas, between the first jejunal loop and the arch of the inferior mesenteric vein or immediately lateral to this vessel, according to the distance of the arch of the inferior mesenteric vein from the jejunum. Toldt's fascia becomes readily visible soon often opening the posterior peritoneum and it appears as a whitish film. After identification of Toldt's fascia, the dissection then proceeds cranially along this plane and in the retro-pancreatic space,

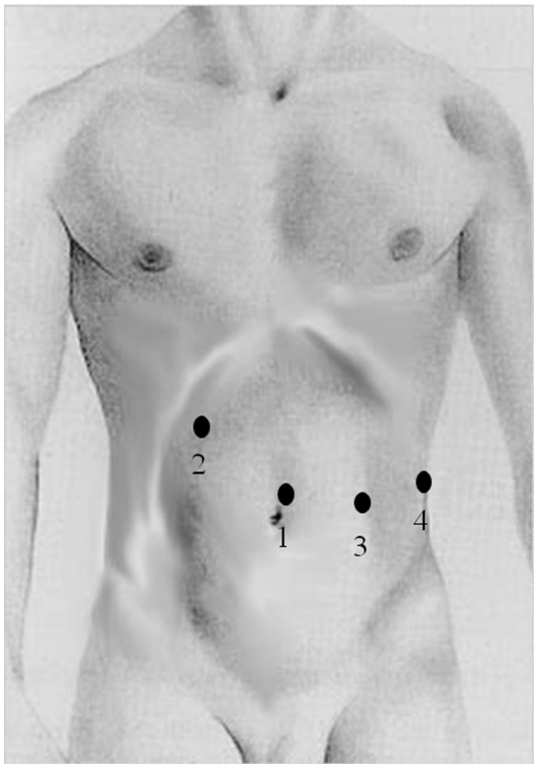

Fig. 1 Trocars' positions during left transperitoneal adrenalectomy. The surgeon and first assistant stand on the left of the patient, while the second assistant stands on the right

after raising the body of the pancreas with an atraumatic instrument by the left hand of the surgeon. The splenic vein can be identified at this point running on the postero-inferior aspect of the pancreas. Next, Gerota's fascia is opened to identify the superior margin of the left renal vein. This is followed medially until its junction with the inferior adrenal vein is identified. The left adrenal vein is then prepared and divided between clips (AcuClip, Tyco/Healtcare, Norwalk, Connecticut, USA). Again, it is worth noting that no manipulation of the left adrenal gland has yet occurred prior to division of the adrenal vein because the gland is located cranially to this vessel. Finally, the gland is mobilized using a radiofrequency (LigaSure™ tissue fusion, Covidien, Mansfield, Massachusetts, USA) or ultrasonic (Ultracision, Harmonic Scalpel, Ethicon Endo Surgery, Cincinnati, Ohio, USA) device and the specimen is then removed from the abdominal cavity inside an extraction bag, after enlarging the periumbilical trocar incision.

Results

There were no significant differences in patients' characteristics (Table 1). Conversion to open surgery was required in 2 cases (3.2 %). Reasons for conversion were

Table 1 Patients' characteristics

	Right anterior approach	Left anterior approach	Left submesocolic approach	Bilateral lesions
Sex ratio (M:F)	12:24	2:3	11:8	2:0
Mean age, years (range)	51.70 (25–84)	45.2 (33–72)	54.2 (23–74)	37 (28–46)
BMI, kg/m^2 (range)	24.1 (19–32)	26.4 (19.6–34)	25.88 (20–32.6)	25.5 (24–27)
Previous abdominal surgery (*n*, %)	8 (22.2)	2 (40)	–	–

BMI body mass index

Table 2 Mean operative time based on tumor size and type of approach

Tumor size (cm)			
Mean operative time, min (range) according to type of approach	0–3	3–6	6–10
Right anterior	102.5 (80–140)	93.4 (55–150)	114.3 (50–240)
Left anterior	155 (50–190)	–	190
Left submesocolic	108.75 (70–195)	98 (60–190)	88.75 (50–115)

dense adhesions between the right adrenal gland and the inferior vena cava (1), and hemorrhage (1). Mean operative time for right and left transperitoneal anterior approach was 101 min (range 50–240) and 163 min (range 50–190), respectively. Mean operative time for left transperitoneal anterior submesocolic approach was 92 min (range 50–195). No differences were observed in operative time depending on the size of the tumor (Table 2). There was a statistically significant difference in mean operative time between the left transperitoneal anterior approach and the left transperitoneal submesocolic approach ($p = 0.0141$). For bilateral LA, the mean operative time was 210 min (200 and 220 min, respectively, for the two patients). Four patients (6.45 %) underwent an associated surgical procedure together with LA (laparoscopic cholecystectomy in 3 cases and a pedunculated uterine fibroid resection in 1), without the need to change the patient's position on the operative table but simply by tilting the operative table, as required for best exposure. Blood pressure was stable during the operation in all cases except six (9.6 %), which was controlled as described above (Fig. 2). Heart rate was likewise stable (Fig. 3).

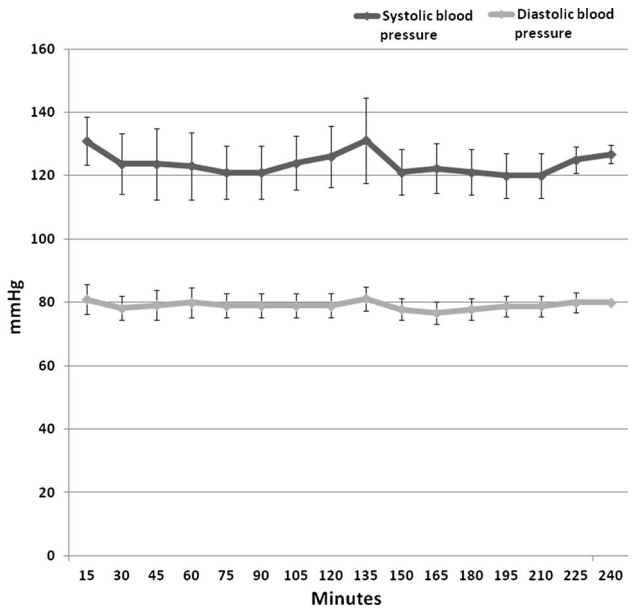

Fig. 2 Intraoperative mean blood pressure and standard deviation

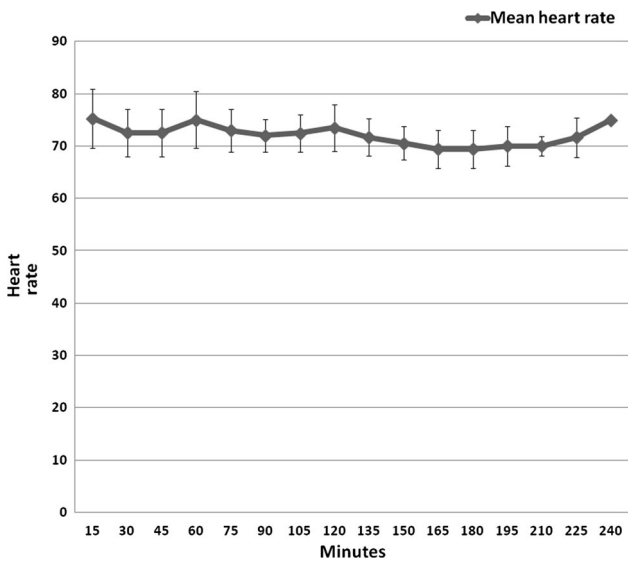

Fig. 3 Intraoperative mean heart rate and standard deviation

Postoperative blood transfusions were required in 4 (6.4 %) patients. Postoperative complications were observed in 4 cases (6.4 %), one Grade III complication according to Clavien's classification [18] (chylous ascites), and 3 Grade I–II complications (pleural effusion 1, anemia 1, pneumonitis 1). Patients' deambulation and resumption of an oral diet occurred on the first postoperative day. Mean hospital stay was 4.8 days (range 2–19). The lesions had a mean diameter of 4.5 cm (range 0.5–10) (Table 3).

Table 3 Results

	Right anterior approach $n = 36$	Left anterior approach $n = 5$	Left submesocolic approach $n = 19$	Bilateral lesions $n = 2$
Conversion rate (%)	2 (5.5)	–	–	–
Complications (Clavien's classification, class)	2 (II)	1 (II) 1 (III)	–	–
Blood transfusions in patients (%)	3 (8.3)	–	–	1
Associated procedures (%)	2 (5.5)	1(20)	–	1
Mean hospital stay days (range)	6.1 (2–11)	7 (2–14)	4.4 (2–8)	13 (7–19)

Discussion

Surgery is the only successful treatment for the treatment of PHE [10, 12, 19]. After the introduction of LA, this has now become the gold standard for adrenal lesions in case of Conn's syndrome, Cushing's disease, incidentalomas, and adrenal metastases [17, 20–22]. Few studies have reported the safety and efficacy of the laparoscopic approach for treatment of PHE [22–24]. The choice of the best minimally invasive approach to the adrenal gland in case of PHE is still debated [20, 25–27].

According to the literature, LA is mostly performed either with a transperitoneal lateral approach or with a retroperitoneal approach [4]. The anterior approach is proposed only by few centers [20, 22]. The transperitoneal lateral approach, originally described by Gagner [4], is performed with the patient in the lateral decubitus position. It gives excellent exposure to both the kidney and the adrenal gland with a wide working space and it facilitates orientation by providing readily identifiable anatomical landmarks [28]. Its proponents report several advantages, such as a rapid and direct access to the gland without the need to retract any organ and with minimal patient trauma [29], a clear operative field due to gravity that keeps blood and bowel away from it, and the need for less surgical dissection on the left side, as compared to the anterior approach [22]. In our opinion, the disadvantages of the lateral approach are that the operative field is narrower than the one provided by the transperitoneal anterior approach. In the flank approach, the first step during left adrenalectomy is the dissection of the lateral and anterior part of the gland, the adrenal vein being identified early during the dissection only in cases of smaller adrenal lesions. In cases

of pheochromocytoma this may lead to intraoperative pressure instability. In a recent meta-analysis, Constantinides et al. report a 4 % conversion rate [30], which is similar to the present series.

The retroperitoneal approach has also been reported to be feasible and safe in the treatment of pheochromocytoma [12, 26, 31]. The posterior retroperitoneal approach is preferred by some, to reduce the risks of a wide abdominal incision and its possible complications, such as wound infection and incisional hernia, as well as complications related to bowel manipulation, such as paralytic ileus [4, 7]. In addition, this technique was reported to require less analgesic therapy due to lower postoperative pain [28]. The retroperitoneal approach has been reported to be associated with earlier recovery of bowel functions, possibly leading to shorter hospital stay and early recovery [28]. This approach is preferred also in patients with abdominal adhesions from previous surgery or in obese patients [32]. Several authors reported a shorter operative time [29]. Walz et al. [33] recommended that a 7 cm hormonally active tumor (occasionally up to 10 cm) or a 4–7 cm non functioning tumor be viewed as indications for a retroperitoneal approach. These authors considered patients with clear signs of malignancy or non resectability, a tumor exceeding 8 (or 10) cm, a concomitant intra-abdominal pathology, or severe obesity as contraindications for this approach [33]. In our opinion, the retroperitoneal approach may increase the operative risk due to a number of considerations. In case of major bleeding, for example, the patient's position is unfavorable for rapid conversion to open surgery. This approach is not indicated if an associated intra-abdominal surgical procedure is required or to explore the contralateral gland. Moreover, the patient's position on the operative table may itself be a direct cause of hemodynamic instability [10]. This approach is also associated with a 4 % conversion rate, and the reported 9 % morbidity rate [30] is higher than in the present series.

To reduce the risk of catecholamines' spread from the adrenal gland, the authors propose a transperitoneal anterior approach with the patient supine as a safe method for the treatment of pheochromocytoma. A significant increase in the rates of plasma norepinephrine release related to mobilization of the adrenal gland has been reported [34]. One study [9] reported that severe hypertension was triggered by direct manipulation of the adrenal gland. LA in the present series was associated with lower morbidity, as compared to other reports [20, 35]. The authors consider early clipping of the main adrenal vein as the first and main target, together with avoiding any manipulation of the gland [20, 22, 36]. In addition, in case of right-sided lesions, there is also a technical reason to prefer right adrenal vein division as the first step of the operation, due to the shortness of the adrenal vein itself. If the gland is mobilized from its surrounding attachments as the first step, the subsequent vascular control is more difficult because the gland tends to be drawn medially and behind the inferior vena cava by the shortness of the right adrenal vein. Instead, early ligation and division of the right adrenal vein after preparation of the medial edge of the gland increase the distance of the gland from the inferior vena cava and facilitates subsequent mobilization of the gland by radiofrequency or ultrasonic instrumentation, since there are no other major vascular structures to control. In the authors' experience, the only disadvantage with the transperitoneal anterior approach on the left side was the wider dissection, and consequently the longer operative time, because the splenic flexure of the colon must be widely mobilized medially to gain access to the adrenal gland. Even the lateral approach requires extensive dissection and mobilization of the spleno-pancreatic complex [4, 37].

For this reason, the authors have introduced transperitoneal anterior left LA via the submesocolic approach, proposed for the first time by Delbet in 1912 [38]. The main advantages of this approach are the limited extent of dissection, reduced operative time due to more direct access to the adrenal vein, and early identification, ligation, and division of the left adrenal vein which is performed prior to any manipulation of the gland. This aspect is particularly important in case of secreting lesions. This approach, however, requires experience in adrenal gland surgery because the operation is conducted in a restricted working space surrounded by major vascular structures, such as the left renal vein, the left splenic vein, and the aorta [27].

In the authors' opinion, LA for pheochromocytoma should be performed only in centers with a well established, multidisciplinary experience in the diagnosis and treatment of adrenal gland pathology, due to the complexity of the disease. In fact, surgery for PHE is at risk of hypotensive or hypertensive crisis, or both, due to an excess in catecholamine release, which cannot be completely prevented even by adequate preoperative preparation with α-blockers [9]. The aim of medical treatment prior to surgery 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 under the best cardiovascular conditions [39]. Advances in intraoperative monitoring and the introduction of preoperative α1 receptors' blockade have radically reduced the mortality rate [34].

Some authors [40, 41] consider tumors larger than 6 cm to be a contraindication for a minimally invasive approach, due to the risk of malignancy. In this series the size of the largest lesion up to 10 cm in diameter did not affect the outcome of the laparoscopic approach or the operative

time. This observation has been confirmed by Parnaby et al. [42], whose results are in agreement with the authors' experience. In the present study, intraoperative blood loss was not correlated with tumor size. The present experience confirms the results of other studies showing the feasibility and safety of LA for pheochromocytoma [13].

Following this surgical strategy, no significant intraoperative change in blood pressure was observed. Based on the present experience, the authors conclude that the anterior laparoscopic procedure for treatment of pheochromocytoma is safe. The transperitoneal anterior approach, moreover, allowed to perform associated procedures without the need to reposition the patient on the operative table. An additional advantage of the transperitoneal anterior access is the opportunity to obtain an intraoperative ultrasound evaluation of the contralateral gland [43] and to perform bilateral adrenalectomy.

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