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Posterior retroperitoneoscopic versus laparoscopic adrenalectomy in sporadic and MENIIA pheochromocytomas

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Abstract

Introduction Retroperitoneal adrenalectomy (PRA) comprises an alternative approach in the management of adrenal tumors that has been set as the treatment of choice in our Institution. We assess the impact of PRA the management of hereditary and sporadic pheochromocytomas comparing its outcomes to the laparoscopic technique, in a case–controlled setting.

Patients and methods From May 2008 to January 2013, 17 patients [5 males and 12 females, mean age: 51 yrs (range 26–73)] with pheochromocytomas underwent PRA. Demographics, tumor characteristics, operative time, complications, hospital stay, and postoperative pain (based on VAS score at days 1 and 3) were compared to 17 selected laparoscopic patient controls [7 males and 10 females, mean age 49 yrs (range 25–64)].

Results 17 patients, 11 with the sporadic form and 6 with MENIIA associated pheochromocytomas, comprised the retroperitoneoscopic group. 19 pheochromocytomas with a mean size 3.7 cm (range 1.7–7.0) at a mean operative time: 105.6 min (range 60–180) were accordingly excised. In the laparoscopic group, 13 patients had sporadic pheochromocytomas, whereas 4 patients had MENIIA syndrome. Mean tumor size of the laparoscopic series was 5.1 cm (range 1.7–8.5) at a mean operative time of 137 min (range 75–195). No mortality or conversions were encountered in both groups. No blood transfusions were needed. Mean visual analog scale pain scores were significantly lower for the retroperitoneoscopic group both on days 1 and 3 [0.94 (0–3) vs 4.15 (3–6), $p < 0.001$ and 0.06 (0–1) vs 3.5 (2–6) $p < 0.001$] respectively. Mean hospital stay for the patients of the retroperitoneoscopic group was significantly better than the laparoscopic group [(2.1 ± 0.24 days vs 40 ± 0.70 days) $p < 0.001$].

Conclusions Retroperitoneoscopic adrenalectomy is associated with excellent clinical results in the management of sporadic and hereditary pheochromocytomas. Moreover, it appears to be superior to the laparoscopic approach, because it is faster and affords the patient with less pain and shorter hospital stay.

Keywords Retroperitoneal adrenalectomy · Pheochromocytoma · MENIIA · Adrenal tumors · Laparoscopic adrenalectomy

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Posterior retroperitoneoscopic adrenalectomy has been recently established as the treatment of choice of the various adrenal tumors in our institution. This decision has been based on various technical and clinical advantages of this method, suggested by our recent work [1] and also by others in the field [2]. Among the technical advantages, the most supportive evidence lies on the direct access, the exclusive retroperitoneal dissection, and the excellent adrenal gland visualization afforded by this operative approach. On clinical grounds, the minimal postoperative pain, the rapid patient mobilization, and the nil blood loss

further enhance the profile of the retroperitoneoscopic technique [3–7].

Pheochromocytomas are rare endocrine tumors that can present insidiously and remain undiagnosed until death or onset of clear manifestations of catecholamine excess. These tumors can no longer be regarded as a uniform disease entity, but rather as a highly heterogeneous group of chromaffin cell neoplasms with different ages of onset, secretory profiles, locations, and potential for malignancy according to underlying genetic mutations. These aspects must be considered, thereby enabling the optimal management of these patients regarding their surgical treatment and the planning of the appropriate post-surgical follow-up and screening especially for those with the hereditary forms of the disease [8, 9].

Under this context, we prospectively compared the results of posterior retroperitoneoscopic adrenalectomy to the laparoscopic adrenalectomy in a series of pheochromocytomas using a case–control setting.

Patients and methods

Patient data—statistical analysis

From May 2008 to January 2013, 17 patients (12 females and 5 males) with sporadic and MENIIA pheochromocytomas underwent posterior retroperitoneoscopic adrenalectomy. The medical records of these patients were reviewed and were compared regarding operative time, complications, hospital stay, and postoperative pain to 17 (10 females and 7 males) laparoscopic patient controls with the same histopathological characteristics. Every effort has been made so that, for a given patient of the retroperitoneoscopic group, a similar patient regarding its demographic and pheochromocytoma tumor characteristics (tumor size, right or left location) was picked up from our laparoscopic pool and was subsequently compared to the patient of the retroperitoneoscopic group. Patients with pheochromocytoma were selected among a pool of 153 laparoscopic adrenalectomies performed between 1997 and 2011.

Preoperative preparation protocol was exactly the same for both retroperitoneal and laparoscopic groups. All patients received the standard regimen of alpha-adrenergic blockage using phenoxybenzamine per os that started 1 week prior to surgery. Adequacy of adrenergic blockage was tested by blood pressure measurements done in supine and erect positions until the patient developed mild orthostatic hypotension. Beta-adrenergic blockage was used selectively on the basis of resting tachycardia >100 b/min. All patients received 3 l of intravenous colloid solution for intravascular volume expansion the day before

surgery. Signed informed consent forms were obtained at the day of surgery.

Perioperative and anesthesia management protocols were the same for both retroperitoneal and laparoscopic groups. During the operation, all patients were routinely monitored using standard American Society of Anesthesiologists methods. These included pulse oximetry, electrocardiography, non-invasive and invasive (through arterial line) blood pressure monitoring as well as end-tidal capnography.

Operative time was recorded by the circulating nurse and corresponded to skin-to-skin time. Pain was assessed by the frequency of postoperative analgesic use and the Visual Analog Pain Scores on postoperative days 1 and 3. The latter was measured using a 1 to 10 scale recorded by the nursing stuff in the patients' wards. Both laparoscopic and retroperitoneal groups received the same postoperative pain management protocol. This consisted of regular (every 6 h) doses of paracetamol/non-steroid anti-inflammatory drug iv plus use of opioids PRN for at least 3 days postoperatively and as long as the patient needed. Patients of both groups were set free to use this scheme of drugs deliberately according to their pain requirements.

Statistical analysis

Relations between categorical variables were examined through the Chi-Square Test (Pearson χ^2). Independent samples t test and the non-parametric Mann-Whitney U test was undertaken to compare mean values of two groups of patients. The assumption for normally distributed variables was examined though Kolmogorov–Smirnov test. Pearson correlations were also estimated. Statistical significance was set at p-value less than 0.05 and all reported values were two-sided. Data analysis was performed with SPSS 17.0 (SPSS, Chicago, IL, USA).

Retroperitoneoscopic group (Table 1): the group consisted of 17 patients, 12 females and 5 males with mean age of 51 years (range 26–73). Six patients had pheochromocytomas associated with genetically proven MENIIA syndrome. This subgroup (RA) comprised of 5 females and 1 male with mean age: 40.7 years (range 26–61). Eleven patients (7 females and 4 males) exhibited sporadic pheochromocytomas (subgroup RB). This group had mean age 56.6 years (range 37–73).

Laparoscopic group (Table 2): in accordance, this group consisted of 17 patients, 10 females and 7 males with mean age of 48.6 years (range 25–64). Four patients (3 males and 1 female) had genetically proven MENIIA syndrome (subgroup LA), with mean age 33 years (range 25–42), whereas 13 patients (4 males and 9 females) had the sporadic form of the disease, (subgroup LB), with mean age 53.4 years (range 45–64).

Table 1 Retroperitoneoscopic group

Gender	Age	Ortime	Loc	Tumor	Post stay	Final histology
M	38	95	LEFT	2	2	PHEO-MEN2A
F	28	80	RIGHT	2.3	2	PHEO-MEN2A
F	28	80	LEFT	2.3	2	PHEO-MEN2A
F	26	80	RIGHT	3.2	2	PHEO-MEN2A
F	45	110	LEFT	2.3	2	PHEO-MEN2A
F	61	90	LEFT	2.7	2	PHEO-MEN2A
F	46	120	BIL R	2.6	2	PHEO-MEN2A
F	46	120	BIL L	2.6	2	PHEO-MEN2A
F	50	90	RIGHT	4	2	PHEO
F	62	90	LEFT	6	2	PHEO
M	50	60	LEFT	4.5	2	PHEO
M	62	150	RIGHT	1.9	2	PHEO
F	55	150	LEFT	6	3	PHEO
M	37	70	LEFT	4.5	2	PHEO
F	71	80	LEFT	2.9	2	PHEO
F	51	110	LEFT	5.5	2	PHEO
F	73	120	LEFT	3.4	2	PHEO
M	66	180	RIGHT	7	2	PHEO
F	46	120	LEFT	1.7	2	PHEO

Table 2 Laparoscopic group

Gender	Age	Or time	Loc	Tumor	Post stay	Final histology
M	42	130	LEFT	2.5	4	PHEO MEN2A
M	34	120	LEFT	4.0	3	PHEO MEN2A
M	25	120	RIGHT	4.5	4	PHEO MEN2A
F	58	100	RIGHT	6.0	5	PHEO
F	49	120	RIGHT	6.5	4	PHEO
M	62	195	LEFT	6.0	4	PHEO
F	58	105	RIGHT	8.5	4	PHEO
M	54	75	RIGHT	5.0	3	PHEO
M	45	170	RIGHT	5.0	4	PHEO
F	48	120	RIGHT	4.5	5	PHEO
F	31	120	LEFT	1.7	3	PHEO MEN2A
M	64	180	RIGHT	6.0	4	PHEO
F	58	155	RIGHT	5.0	5	PHEO
F	53	150	RIGHT	7.0	3	PHEO
F	50	170	LEFT	4.5	4	PHEO
F	46	150	LEFT	5.3	5	PHEO
F	49	150	LEFT	5.1	4	PHEO

Operative procedure

Retroperitoneoscopic adrenalectomy is performed according to principles described in detail by Walz et al. (2) and by us (1). The operation is carried out under general anesthesia with the patient in prone position supported on mattresses. An arterial catheter, a nasogastric tube and a urinary catheter are always used.

The operation commences with a 1.5-cm incision placed just below the tip of the 12th rib. After sharp dissection of the subcutaneous and muscle tissues, the dorsolumbar fascia (Gerota's fascia) is reached and subsequently sharply perforated. Special care is needed so that the opening should have the right size to accommodate a 10 mm blunt tip trocar but not to be large enough allowing carbon dioxide escape. 5- and 10-mm reusable trocars are then placed under direct finger guidance, the former 4–5 cm laterally toward the midaxillary line, and the latter just next to the sacrospinal muscles. Finally, a disposable 10 mm blunt tip trocar is introduced through the initial incision site. Insufflation of carbon dioxide starts from this trocar maintaining a CO_2 pressure within a range of 25 to 30 mmHg. Retroperitoneoscopy is performed with a 10 mm 30° camera initially introduced through the medial trocar.

The first operative step involves the creation of a cavity by pushing away the retroperitoneal fatty tissue toward the Gerota's fascia. This step is accomplished with blunt dissection and is almost bloodless. Subsequently, the camera is placed through the sacrospinal trocar and the dissection begins using ultrasonic scissors.

At this time, the adrenal gland tumor can be visualized but the major concern is to find the upper kidney pole. After that, the fatty tissue between kidney and adrenal gland is sharply separated. From then on, all efforts are focused on the adrenal vein. On the right side, the vein is short and is found in posterolateral position on the posterior surface of the vena cava. On the left side, the adrenal vein is long and lies caudally, medially to the upper kidney pole. After adrenal vein ligation, dissection proceeds in a fairly easy manner using ultrasonic scissors. After complete excision of the adrenal gland, extraction is accomplished with a retrieval bag system. No drains are placed. Fascia and skin closure are carried out in a usual way with absorbable sutures.

Results

No conversions were encountered in both retroperitoneoscopic and laparoscopic groups.

Retroperitoneoscopic group

19 pheochromocytomas on 17 patients, 12 located on the left side and 7 on the right side, were excised by the posterior approach (two bilateral cases). Mean size of the posterior excised pheochromocytomas was 3.68 cm (range

1.7–7.0). Mean size of the left adrenal tumors was 3.84 cm (range 1.7–6.0) and 3.5 cm (range 1.9–7.0) for the right tumors. Mean operative time for the retroperitoneoscopic group was 105.6 min (range 60–180). Right retroperitoneal adrenalectomies were carried out in mean operative time of 117 versus 100 min for the left ones, so no significant difference between the operated sites was recorded ($p = 0.305$). The average days of hospital stay were 2.1 (range 2–3). The average Visual Analog Pain Scores on days 1 and 3 were equal to 0.94 (range 0–3) and 0.06 (range 0–1), respectively.

Retroperitoneoscopic MEN2A group (subgroup RA)

Six patients (5 females and 1 male) had pheochromocytomas associated with genetically proven MENIIA syndrome: Mean tumor size was 2.5 cm (range 2.0–3.2) and mean operative time was 95.8 min (range 80–120). All patients stayed in the hospital for 2 days.

Retroperitoneoscopic sporadic group (subgroup RB)

Eleven patients (7 females and 4 males) exhibited sporadic pheochromocytomas. This group had mean tumor size 4.3 cm (range 1.7–7) and mean operative time 111 min (range 60–180). All patients stayed in the hospital for 2 days, except one patient who stayed 3 days.

Laparoscopic group

17 pheochromocytomas, 10 located on the right side and 7 on the left side, were excised by the anterior laparoscopic approach. Mean size of the excised pheochromocytomas of the laparoscopic series was 5.12 cm (range 1.7–8.5). Mean size of the left adrenal tumors was 4.16 cm (range 1.7–6.0) and 5.8 cm (range 4.5–8.5) for the right tumors. Mean operative time for the laparoscopic series was 137.1 min (range 75–195). Right laparoscopic adrenalectomies were carried out in mean operative time of 130 min (range 75–180) versus 148 min (range 120–195) for the left ones. The average days of hospital stay were 4 (range 3–5). The average Visual Analog Pain Scores on days 1 and 3 were equal to 4.2 (range 3–6) and 3.5 (range 2–6), respectively.

Laparoscopic MEN2A group (subgroup LA)

Four patients (3 females and 1 male) had pheochromocytomas associated with genetically proven MENIIA syndrome. Mean tumor size of this subgroup was 3.18 cm (range 1.7–4.5) and mean operative time was 123 min (range 120–130). The average days of hospital stay were 3.5 (range 3–4).

Laparoscopic sporadic group (subgroup LB)

Thirteen patients (9 females and 4 males) had sporadic pheochromocytomas. Mean tumor size was 5.7 cm (range 4.5–8.5) and mean operative time was 142 min (range 75–195). The average days of hospital stay were 4.2 (range 3–5).

Intraoperative transfusion was never needed in either retroperitoneoscopic or laparoscopic approaches. The same was true for drainage, as it never deemed necessary in both procedures. Regarding the posterior endoscopic method, given the awkward position of the patient, circulation instability never occurred and all patients with pheochromocytomas had an uneventful intra- and postoperative course hemodynamic wise.

Operative time was significantly shorter for the retroperitoneal series {mean retroperitoneal operative time: 105.6 min (range 60–180) versus mean laparoscopic operative time: 137.1 min (range 75–195) $p = 0.007$}.

Pearson analysis showed very weak correlation of the operative time with the patients' age (correlation coefficient 0.277, p-value $= 0.113$). The same analysis done for the effect of tumor size on the operative time, showed borderline significance (correlation coefficient 0.322, p-value $= 0.063$). The correlation among the tumor size and the day 1 and day 3 VAS scores was not statistically significant (p-values equal to 0.214 and 0.342, respectively).

In regards to the effect of Body Mass Index on the operative time, the lack of laparoscopic BMI data did not allow for direct comparison between these groups.

As far as complications concerned, a constant intraoperative finding of the retroperitoneoscopic series was the cutaneous emphysema and eye lid edema that occurs in most patients operated by this approach. This cutaneous emphysema resolved spontaneously in all patients within the first 6 h, without any other untoward clinical consequences.

Postoperative pain assessed by the frequency of analgesic use and the Visual Analog Pain Scores on days 1 and 3 was significantly lower for the retroperitoneoscopic group. Mean Visual Analog Scale pain scores were significantly lower for the retroperitoneoscopic group both on days 1 and 3: [0.947 (0–3) vs 4.1 (3–6), $p < 0.001$] and [0.06 (0–1) vs 3.5 (2–6) $p < 0.001$] respectively. Postoperative analgesia for this group was required only for the first 24 h by means of paracetamol and one or two doses of NSAID drug. Patients of the laparoscopic group needed regular doses of the same scheme of drugs for much greater time (4–5 days) plus regular doses of opioids, especially during the first 48 h.

Mean hospital stay for the patients of the retroperitoneoscopic group was significantly better than that of the laparoscopic group [2.1 ± 0.24 days vs 4.0 ± 0.7 days, $p < 0.001$]. No correlation has been found between the

Fig. 1 Retroperitoneal vs Laparoscopic operative time
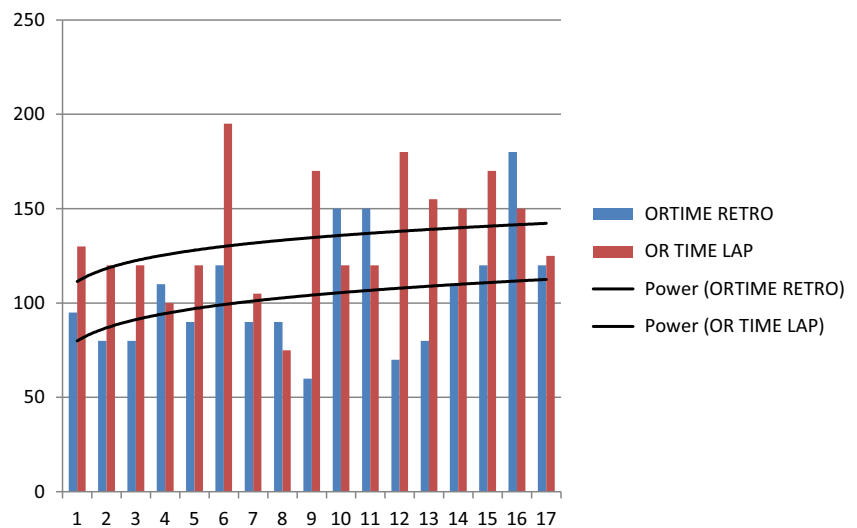
patients' age (p-value $= 0.226$) or tumor size (p-value $= 0.507$) with the hospital stay.

No mortality was encountered in both groups. A specific postoperative complication associated with the posterior approach was a lateral abdominal swelling that occurred in 2 patients and persisted for several days (in one patient this swelling resolved in 6 weeks) without any other clinical effect. There was one case of postoperative abdominal wall hernia in the laparoscopic group. We had no problems with wound healing and cosmetic results were excellent especially in the retroperitoneoscopic group.

Discussion

Posterior retroperitoneoscopic adrenalectomy has been associated with a significant benefit in pain medication requirement, time of patient recovery, and length of hospital stay in this series. The superiority of retroperitoneal adrenalectomy compared to the laparoscopic approach in terms of significantly less postoperative pain, shorter convalescence time, and shorter hospital stay has been previously demonstrated both in our (1) as well as numerous other comparative studies in the literature [2, 10–15]. In this paper, it is also clearly showed that the posterior adrenalectomy preserve its superior characteristics even in pheochromocytomas, a well-known challenging adrenal pathology [16, 17]. In general, these tumors tend to be larger than other adrenal functional or non-functional tumors and very often exhibit increased vascularity with fragile vessels that tend to bleed with minimal manipulation. For this reason, we avoid excessive tumor manipulation and we rely on meticulous clips and ultrasonic sealing scissors application for hemostasis.

Surprisingly enough, a significantly shorter operative time was recorded for both right or left sides in retroperitoneal adrenalectomy (Fig. 1). Even though the mean size of the excised tumors by the laparoscopic approach appear to be significantly larger than that of the retroperitoneal approach (5.12 vs 3.67, $p = 0.014$) and may contribute to this result, (although no statistically significant correlation was found between the tumor size and the operative time, or the pain scores for both groups), some other factors must be taken into account. First, the establishment of pneumoperitoneum and the insertion of multiple trocars seems to be logically lengthier than the digitally creation of the retroperitoneal space and the insertion of less trocars. Second, the direct access offered by the retroperitoneal approach is clearly superior to the laparoscopic approach especially on the left adrenalectomies in which the lengthier operative time of the latter may perhaps be attributed to the retraction and mobilization of intra-abdominal organs needed for adequate exposure, which may also be a source of significant morbidity. On the right side, in which the dissection and the ligation of the right adrenal vein constitutes the most critical operative step of the right adrenalectomy, we believe that the visualization and the control of the right adrenal vein afforded by the posterior approach is beyond comparison. The reason lies on the exemplary visualization and dissection of the posterior surface of the vena cava that allows for precise control of the right adrenal vein at its take off at the posterolateral aspect of the vena cava (Fig. 2). Moreover, the right retroperitoneal approach allows for easier identification and ligation of the numerous vessels that come directly from the aorta/vena cava at the lower aspect of the right adrenal gland.

The effect of tumor size in the operative time of the retroperitoneal approach has been proved to be marginally

Fig. 2 Retroperitoneal view of the posterior surface of the vena cava and the take off of the right adrenal vein during the retroperitoneoscopic adrenalectomy

significant. However, no correlation has been found between the tumor size and the postoperative pain levels or hospital stay in this series. Thus far, the largest excised pheochromocytoma in this series was 7 cm and it was associated with the lengthier operative time. Nevertheless, the upper tumor size that can be excised by the retroperitoneal approach is difficult to be precisely set. On strict technical grounds, since the extraction of the specimen is done through the 10-mm trocar site and no morcellation is used, the specimen size becomes a critical factor in regards to the length of the skin incision needed to extirpate the tumor. In addition, factors such as the surgeon's experience and technical competence may also play a significant role. Nevertheless, we believe that extirpation of tumors bigger than 7 cm may somehow defeat the purpose of a truly minimally invasive procedure especially if no morcellation is used.

Intraoperative cardiovascular instability with episodes of sudden and severe hypertension, especially in regards to the awkward patient position, never happened. This can be attributed to the adequate preoperative alpha-adrenergic blockage, but most importantly, to the continuous invasive monitoring and pharmacologic intervention offered by our experienced anesthesiology team. Additionally, in the case of retroperitoneal adrenalectomy, the role of the anesthesiology support is of paramount importance for one more reason: the retroperitoneal absorption of the CO_2 is quite high, probably due to the higher pressures used, so close monitoring and correcting measures against the buildup of high levels of arterial CO_2/acidosis or the appearance of cutaneous emphysema must be early instituted. Given this experienced support, there were no serious events in this series.

MENIIA pheochromocytomas exhibit no difference than the sporadic tumors in both procedures. Retroperitoneal approach was used with excellent results in two bilateral cases. The prone position of the patient in this case facilitates the access to both sides simultaneously, obviating the need for repositioning during the procedure.

Conclusions

Retroperitoneoscopic adrenalectomy is associated with excellent clinical results in the management of sporadic and hereditary pheochromocytomas. Moreover, it is clearly superior to the laparoscopic approach, because it is faster and affords the patient with less pain and shorter hospital stay.

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