



Laparoscopic resection of giant adrenal malignant tumors, a case series and review of the literature

Konstantinos Sapalidis¹, Christoforos Kosmidis¹, Dimitrios Giannakidis¹, Varvara Fyntanidou², Anastasios Barmpas¹, Paul Zarogoulidis¹, Athanasios Katsaounis¹, Charilaos Koulouris¹, Nikolaos Michalopoulos¹, Aikaterini Amaniti², Zoi Aidoni¹, Stelian Mogoanta³, Michael Karanikas⁴, Panagoula Oikonomou⁵, Konstantinos Romanidis⁵, Anastasios Vagionas⁶, Alexandru Marian Goganau⁷, Alexandru Munteanu¹, Valeriu Surlin¹, Isaak Kesisoglou¹

¹3rd Department of Surgery, ²Anesthesiology Department, “AHEPA” University Hospital, Aristotle University of Thessaloniki, Medical School, Thessaloniki, Greece; ³Department of Surgery, Faculty of Dentistry, University of Medicine and Pharmacy of Craiova, Craiova, Romania; ⁴Department of Surgery, Democritus University of Thrace, Dragana, Alexandroupolis, Greece; ⁵Second Department of Surgery, University Hospital of Alexandroupolis, Medical School, Democritus University of Thrace, Alexandroupolis, Greece; ⁶Oncology Department, General Hospital of Kavala, Kavala, Greece; ⁷General Surgery Clinic 1, University of Medicine and Pharmacy of Craiova, Craiova County Emergency Hospital, Craiova, Romania

Correspondence to: Paul Zarogoulidis, MD, PhD. 3rd Department of Surgery, “AHEPA” University Hospital, Aristotle University of Thessaloniki, Medical School, Thessaloniki, Greece. Email: pzarog@hotmail.com.

Abstract: Laparoscopic approach for suspected adrenal malignancies remains a controversial issue and it gets more controversial, when managing giant adrenal malignant tumors. The aim of this paper is to present five cases of patients with giant adrenal malignant tumors that underwent laparoscopic transabdominal lateral adrenalectomy in our department between 2010 and 2017. Literature is also reviewed in order to investigate the feasibility of laparoscopic resection in these cases.

Keywords: Giant adrenal tumors; laparoscopic adrenalectomy; transabdominal lateral position; outcomes

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Introduction

Adrenal carcinomas are rare and aggressive malignancies (1). Laparoscopic approach, although a gold standard for benign adrenal tumors, is not reserved for malignant diseases. Since large tumor size bears the possibility of malignancy, it seems even challenging when treating such masses laparoscopically (2). Certainly an oncology council should provide a solution for these patients, however; most of the times the histology confirmation comes after the surgery. Biopsy of these lesions might also spread the disease in surrounding tissue. Therefore experience is needed and these types of surgeries should be performed in specific centers. In this short case series, the outcomes of laparoscopic approach for large malignant adrenal tumors are reported.

Case presentation

Between 2010 and 2017, 64 patients with adrenal tumors were hospitalized and treated in our Department. Five of them were diagnosed with malignant adrenal tumors (*Table 1*). Accurate preoperative diagnosis was set in one of the patients. This patient was diagnosed with Cushing’s syndrome. On MRI a large adrenal mass and two metastatic liver lesions were observed. For the other patients, preoperative imaging studies were inconclusive and they had nonfunctioning tumors (*Table 2*).

It is remarkable that the mean size of the tumors was 12.7 cm with a range from 8 to 16 cm. For all of them laparoscopic excision was offered. Lateral transabdominal position was preferred from retroperitoneal approach

Table 1 Perioperative complications, histology, patterns of recurrence and follow-up in 5 patients

Patient	Perioperative complications	Histology	Site(s) of first recurrence	Status [months of follow-up]
1	None described	Mixed corticomedullary carcinoma	No recurrence was noticed	Dead [6]
2	None described	Malignant paraganglioma	Local recurrence	Alive with disease [12]
3	None described	Adrenal cortical carcinoma	No recurrence was noticed	Dead [8]
4	None described	Adrenal cortical carcinoma	No recurrence was noticed	Dead [12]
5	None described	Metastatic undifferentiated carcinoma	–	Alive with disease [12]

Table 2 Demographics, clinical presentation, tumor characteristics in 5 patients

Patient	Sex/Age	Signs and symptoms	Hormone production	Side	Computed tomography/magnetic resonance characteristics	Size (cm)
1	M/63	Weight loss, abdominal pain	None	Left	Enhanced heterogeneous mass with indeterminate borders	8×7.5×4.5
2	M/45	Pain	None	Right	–	16×13×7
3	F/32	Weight gain, pain	None	Right	Slightly heterogeneous mass with indistinct medial border	11×11.5×4.5
4	F/58	Weight gain, arterial hypertension	Cortizol alone	Right	Heterogeneous mass with indistinct borders	15×5.8×2.7
5	F/80	Abdominal pain, anemia	None	Right	–	13×6.5×5.5

because of the advantage of the first to explore beyond the ipsilateral gland and evaluate the organs of the peritoneal cavity for metastatic lesions and take biopsies if needed. Furthermore, it allows inspection of the contralateral gland and ‘en bloc’ excision in case of infiltration to the adjacent tissues, gives more working space and allows a good exposure during the removal of the adrenal gland. However, the retroperitoneal approach may be associated with less intra-operative complications and shorted operation time but in our case those drawbacks were eliminated from the experience and the technical excellence of the surgical team.

One procedure was converted to open, since the lesion penetrated the surrounding tissue and it was impossible to achieve total resection laparoscopically.

Operative time was 105 to 170 minutes. There was minimal blood loss in all patients and no need for transfusion. On one occasion, incision was enlarged in order to facilitate the removal of the surgical specimen. The mean postoperative hospital stay from 1 to 5 days (mean, 3 days) (*Figure 1,2*). There were no perioperative complications (*Table 1*).

On histology two cases were reported as adrenocortical

carcinomas and one as mixed carcinoma (both cortical and medullary). One tumor was metastatic with unknown origin. This patient was referred for further investigation with PET scan since no primary lesion was observed on CT and MRI scans. The last case, which was the converted case, was a malignant paraganglioma. To all patients oncological reference was provided after the histology report. During follow up one case of incisional hernia and one recurrence were observed. Recurrence was noticed for the patient with the paraganglioma.

Discussion

Primary adrenocortical carcinomas are extremely rare with an estimated annual incidence of about 2 cases per million people (1,3). They may present as a hormone-secreting or inactive tumors. In both instances, most patients are diagnosed at an advanced stage (4). The most common adrenal malignant lesion is metastases. Adrenal metastases are usually bilateral, but may also be unilateral as it was reported in our series. They are present at autopsy in up to 27% of patients with known malignant epithelial tumours.

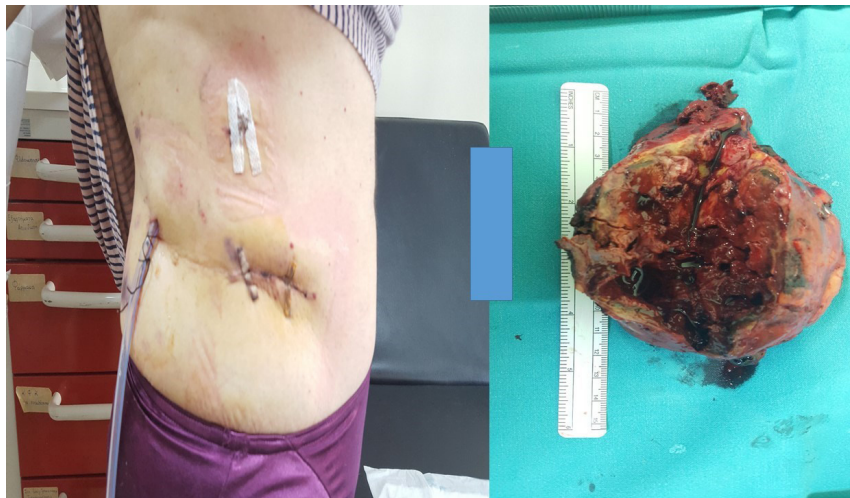


Figure 1 First patient second post-surgery day (left) and the tumor on the right.

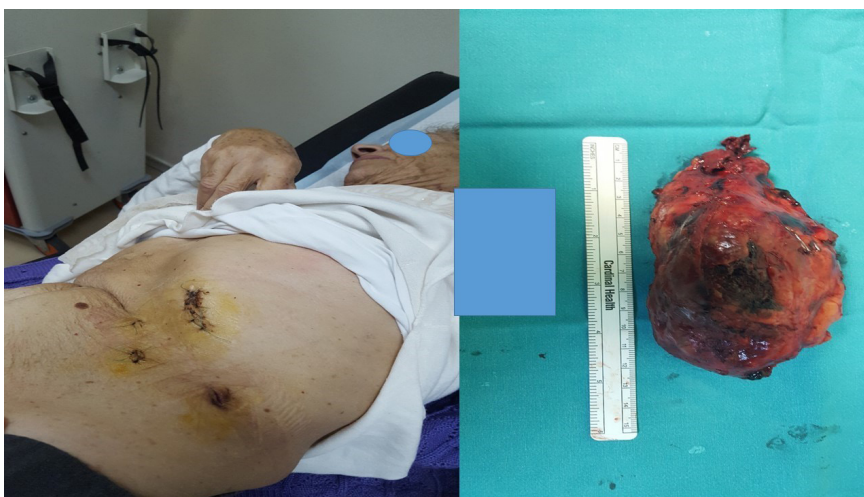


Figure 2 Second patient second post-surgery day (left) and the tumor on the right.

Common primary malignancies include lung, colorectal and renal cancer.

Based on the recommendations of the European Network for the Study of Adrenal Tumors (ENS@T) a pre-operative hormonal workup for suspected ACC. Usually, biochemical assessment is targeted to exclude the diagnosis of pheochromocytoma, and determine the excessive secretion of steroids/precursors (especially cortisol). Supplementarily, a thoracoabdominal CT with contrast injection within at least 6 weeks before adrenalectomy for suspected ACC is recommended. MRI with gadolinium enhancement is required in patients with doubtful diagnosis,

suspected vascular invasion or liver metastasis ENSAT GUIDELINES (5). However, no single imaging method can characterize a localized adrenal mass as ACC. It is important to note that in many patients the ACC diagnosis is confirmed only after surgery; hence the surgical strategy is based on a supposed diagnostic procedure.

This raises the dilemma on which surgical procedure to choose. Considering the aggressiveness of the tumor, the only chance for patients is complete margin-free primary tumour resection, avoiding violation of the tumour capsule or spillage of tumour cells (4,6). Until recently, a lack of standardization for the surgical approach is seen. Current

Table 3 Laparoscopic versus open adrenalectomy for large adrenal malignancies

Author/year	LAP/ open	Mean size LAP/open (cm)	Conclusion
Gonzalez/2005	6/153	6/13	"Laparoscopic resection of ACC is associated with a high risk of peritoneal carcinomatosis. Open adrenalectomy remains the standard of care for patients presenting with an adrenal cortical tumor for which ACC is in the differential diagnosis"
Nocca/2007	4/5	8.5/12.2	"Laparoscopic removal of a corticoadrenaloma should not worsen the prognosis, provided the surgeon respects the primary rules of oncologic resectional surgery. Any surgical conditions that would preclude the strict application of these criteria are contraindications to a laparoscopic procedure"
Porpiglia/2010	18/25	9/10.5	"OA and LA may be comparable in terms of recurrence-free survival for patients with stage I and II ACC when the principles of surgical oncology are respected"
Miller/2010	17/71	6/12.3	"Although feasible in many cases and tempting, laparoscopic resection should not be attempted in patients with tumors suspicious for or known to be adrenocortical carcinoma"
Leboulleux/2010	6/58	6.9/14	"Increased risk of PC after LA for ACC. Whether this is related to an inappropriate surgical approach or to insufficient experience in ACC surgery should be clarified by a prospective program."
Brix/2010	35/117	6.2/8	"For localised ACC with a diameter of <10 cm, LA by an experienced surgeon is not inferior to OA with regard to oncologic outcome"
Lombardi/2010	30/126	7.3/9	"The operative approach does not affect the oncologic outcome of patients with localized adrenocortical carcinoma, if the principles of surgical oncology are respected"
Mir/2011	18/26	7/13	"A non-statistically significant increase in recurrence and death was observed among patients undergoing LA versus OA after adjusting for clinical stage. The rarity of this disease limits the ability to assess for significant differences in a single-institution series. Patients with suspected ACC should be considered for OA"
Donatini/2011	13/21	5.5/6.8	"LA was associated with a shorter length of stay and did not compromise the long-term oncological outcome of patients operated on for stage I/II ACC B 10 cm ACC. Our results suggest that LA can be safely proposed to patients with potentially malignant adrenal lesions smaller than 10 cm and without evidence of extra-adrenal extension"
Cooper/2012	46/46	8/12.3	"Despite typically being performed in patients with smaller tumors, laparoscopic adrenalectomy for ACC is associated with higher rates of recurrence, particularly peritoneal recurrence. For patients with known or suspected ACC, the oncologic benefits of open resection outweigh the short-term benefits of minimally invasive surgery"
Fossa/2013	17/15	8/13	"LS seems to offer short-term advantages and similar long-term outcome compared to OS in patients with resectable ACC stage I-III"
Zheng/2018	20/22	6.3/10.1	"OA for adrenocortical carcinoma is superior to laparoscopic approach in terms of DFS and rate of 2-year DFS, in spite of the larger maximum diameter of tumors and lesser benefit during perioperation. After LA, patients are more likely to show local recurrent lesions at the first time of relapse."

knowledge is based on retrospective studies and expert opinion. No randomized trials comparing laparoscopic and open approaches exist. The published retrospective studies report conflicting results (Table 3). Leboulleux *et al.* (7), Gonzalez *et al.* (8), Miller *et al.* (9), Mir *et al.* (10), Cooper *et al.* (11) and Zheng *et al.* (12) are reluctant to use the

laparoscopic approach for ACC. Gonzalez *et al.* observed frequent local and peritoneal recurrence, Leboulleux *et al.* (7) found that laparoscopic approach was the only predictive factor of peritoneal carcinomatosis while Zheng *et al.* (12) concluded on higher frequency of local recurrence. Miller *et al.* showed that disease-free intervals were shorter

in patients undergoing laparoscopic adrenalectomy. No one of them could distinguish the risk of recurrence due to an inappropriate surgical approach or due to an inexperienced surgeon.

On the other side, Nocca *et al.* (13), Brix *et al.* (14), Porpiglia *et al.* (15), Lombardi *et al.* (16), Donatini *et al.* (17) and Fossà *et al.* (18) support that the laparoscopic approach not only offers the benefits of laparoscopy but also does not affect the oncological outcome. All of them highlight the significance of respecting the rules of oncologic surgery especially for localized ACC with a diameter inferior to 10 cm.

However, no definite conclusion can be given due to their retrospective nature. Moreover, the restricted heterogeneous number of cases, the lack of standardization of the surgical procedure and the short follow-up period complicates a safe conclusion. The majority of these studies agree that a multicenter surgical working panel should be held in order to initiate a prospective trial so as to define the optimal surgical management of adrenal malignancies. In our perspective, laparoscopic transabdominal lateral adrenalectomy is a feasible surgical technique for excision of giant adrenal malignant tumors when rules of oncologic surgery are respected (R0) from experienced and technically excellent surgical teams. Furthermore, despite of recent updates in terms of adjuvant treatment, with mitotane and newer chemotherapy protocols complete local excision has been the only curative treatment. Moreover, from our experience the oncologic outcome is not affected by the operative approach if the principles of oncologic surgery are respected.

Conclusions

Due to the scarcity of the tumor, the lack in preoperative diagnostic procedures and the absence of guidelines in surgical treatment patients with adrenal malignancies should be treated in referral centers by experienced surgeons. In such cases, laparoscopic adrenalectomy of large adrenal malignancies can be feasible in terms of surgical oncology.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest

to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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