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Current role of open surgery in adrenal tumors

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SUMMARY: **Current role of open surgery in adrenal tumors.**

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Aim. *The aim of this retrospective evaluation is to assess the current role of open adrenalectomy, in particular in cases of adrenocortical carcinoma (ACC).*

Materials and methods. *From January 2009 to May 2019, 26 open out of 233 adrenalectomies were performed in our Academic Department. Open adrenalectomy was performed by the anterior approach. A midline abdominal incision or a subcostal surgical incision was used to reach the peritoneal cavity. The resection was defined R0 if the margins of the sample were negative for malignancy.*

Results. *Open adrenalectomy was performed in 26 patients: 10 men and 16 women with a mean age of 61±25.3 years and a mean BMI of 28.4±2.9. The right adrenal gland was removed in 15 cases and the left in 11 cases.We reported 18 diagnosis of malignant pathology. The other diagnosis concerned 5 cases of pheochromocytoma, 1 case of Cushing's disease and 2 cases of hyperaldosteronism. Mean tumor size was 7.7±5.5. Mean operative time was 160 min (range=110-205 minutes). Mean postoperative stay was 7±2 days. Only 3 (10%) patient showed postoperative grade II complications, according to Clavien-Dindo classification. Midline abdominal incision was used in 18 patients, subcostalsurgical incision in 5 patients and bilateral subcostal surgical incision in 3 patients. 3 right nephrectomy was necessary to remove the entire tumor mass. An en bloc R0 tumor resection was accomplished in all cases.There was no intra and perioperative mortality. All patients recovered well from surgery. The mean follow-up period was 15 (range=6-48) months.*

Conclusion. *In conclusion, our retrospective study points out the role of open adrenalectomy as the treatment of choice in selected cases with known or suspected malignant adrenal tumors and with size greater than 12 cm.*

KEY WORDS: Open adrenalectomy - Adrenal gland - Surgery.

Introduction

Minimally-invasive adrenalectomy has become the treatment of choice for benign adrenal lesions thanks to several advantages, such as faster recovery, shorter hospitalization, and rapid return to normal activities (1, 2). Nevertheless, actually, there is a consensus that open adrenalectomy still plays an important role for the treatment of large or malignant tumors potentially infiltrating adjacent organs. In particular, the main indications to open adrenalectomy are large adrenocortical tumors (>6-8 cm) and those with CT that shows locally invasive tumors (3). Moreover, minimally-invasive adrenalectomy should be converted to open technique in case of macroscopic signs of malignancy (invasion in surrounding structures, presence of regional lymphadenopathy) or if there is the risk of tumor fragmentation/spillage and also in case of intraoperative accidents (e.g., massive bleeding) uncontrollable with minimally-invasive technique. In addition, guidelines strongly recommend an open adrenalectomy for large or invasive pheochromocytomas (8-10 cm) in order to perform a complete tumor resection, to prevent a lesion rupture and to avoid a local recurrence (4, 5). The aim of this retrospective evaluation is to assess the current role of open adrenalectomy, in particular in cases of adrenocortical carcinoma (ACC).

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Material and methods

From January 2009 to May 2019, 26 open out of 233 adrenalectomies were performed in our Academic Department. Biochemical evaluation included screening for cortisol overproduction, catecholamine and aldosterone dosing. Sex hormones were evaluated in anyone with virilizing features or imaging characteristics suspicious for ACC. Imaging included an adrenal protocol CT or MRI. Patients with pheochromocytomas underwent a pre-operative treatment with alpha-blockers or in particular cases with beta-blockers, while patients with Cushing's disease underwent a cortisone-based therapy. Open adrenalectomy was performed by a single surgeon, using the anterior approach. A midline abdominal incision or a subcostal surgical incision was used to reach the peritoneal cavity. The resection was defined R0 if the margins of the sample were negative for malignancy.

Results

Open adrenalectomy was performed in 26 patients: 10 men and 16 women with a mean age of 61±25.3 years and a mean BMI of 28.4 ±2.9. 15 right and 11 left adrenalectomies were performed. We reported 18 diagnosis of malignant pathology: 15 cases of adrenal cancer and 3 cases of metastasis, including one from renal cell cancer, one from lung cancer and one from breast cancer (Table 1). The other diagnosis concerned 5 cases of pheochromocytoma, 1 case of Cushing's disease and 2 cases of hyperaldosteronism. In particular, in 2 patients affected with pheochromocytoma CT imaging concerned for malignancy, while in remaining 6 patients CT imaging concerned for large lesions (Table 2). Mean tumor size was 7.7±5.5 cm. In detail, in 6 patients, affected with benign lesions, mean tumor size was 15,1±2,75 cm, while in 20 patients this was 5,4±3,5 cm associated with radiologic imaging features concerning for malignancy. Mean operative time was 160 min (range=110-205 minutes). Mean postoperative stay was 7±2 days. 3 (10%) patient showed postoperative grade II complications, according to Clavien-Dindo classification (post-operative anemia treated with blood transfusions). Midline abdominal incision was used in 18 patients, subcostal surgical incision in 5 patients and bilateral subcostal surgical incision in 3 patients because of their high BMI. 3 right nephrectomy was necessary to remove the entire tumor mass. An *en bloc* R0 tumor resection was accomplished in all cases.There was no intra and perioperative mortality. All patients recovered well from surgery. Mean follow-up period was 15 (range=6-48) months (Table 1).

TABLE 1 - PATIENT DEMOGRAPHICS AND CLINICAL OUTCOME.

Sex M/F	10/16
Median age	61,5±25,3
BMI	28,4±2,9
Side R/L	15/11
Size (cm)	7,7±5,5
Diagnosis	
- *Pheochromocytoma*	5
- *Cushing's disease*	1
- *Hyperaldosteronism*	2
- *Adrenal cancer*	15
- *Metastatic disease*	3
Mean operative time (min, range)	160 (110-205)
Complication (N°/grade Clavien-Dindo)	3/II
Mean postoperative stay	7±2
Abdominal incision	
- *Midline*	18
- *Subcostal*	5
- *Bilateral subcostal*	3
Extended multiorgan resections	3 right nephrectomy
Mortality	-
Follow up (months)	15 (range=6-48)

Discussion

Adrenocortical carcinoma (ACC) represents a rare and aggressive malignancy, in most cases presenting at an advanced stage. The estimated incidence of adult ACC is between 0.7 and 2.0 per million per year. ACC occurs at any age with a peak incidence between 40 and 60 years, and with a higher prevalence in female population (55-60%). The median overall survival is 3-4 years (6, 7). Staging classification for adrenocortical carcinoma and TNM criteria was defined by the International Union Against Cancer first in 2004 and then modified in 2009. Five-year survival is 60-80% in case of tumor confined to the adrenal space, 35-50% for locally advanced disease, 0% to 28% in case of metastatic disease (8). Metastases are common, including liver, kidney, and vena cava on the right side and pancreas, spleen, renal vein, and kidney on the left side. Moreover, vena cava tumor thrombus is common, often originating at the level of the right adrenal vein and extending into the retrohepatic cava or extending from the left renal vein into the infrahepatic vena cava. Regional lymphadenopathy may also be seen (9). In view of the complexity of the pathology, every kind of adrenal lesion should be referred to a multidisciplinary evaluation, to share the indication with expert endocrinologists, radiologists and pathologists, together with dedicated surgeons. In stages I-III, complete surgical resection represents the only means of cure (10). Minimally invasive adrenalectomy is safe and significantly superior to open surgery above all in terms of hospital stay, blood loss, lower rate of complication and better cosmetic results (11, 12). In addition, this approach allows an excellent visualization thanks to the magnification of the laparoscope, and the access to the anatomic region which otherwise requires an extensive transperitoneal approach (13). The main indications to minimally invasive adrenalectomy are above all small benign functioning tumors or pheochromocytomas without signs of malignancy, incidentalomas or metastases in selected case (14, 15). However, an incomplete resection of malignant adrenal tumor carries a poor prognosis (median survival is less than 12 months) (7). In our Academic Department, which is part of a Referral Center for Adrenal Diseases and Secondary Hypertension, 26 patients underwent open adrenalectomy. 15 right and 11 left adrenalectomies have been carried out, with a mean operative time of min 160 (range=110-205 minutes). We reported 3 cases of metastasis, including one from renal cell cancer, one from lung cancer and one from breast cancer, all treated with mini-invasive approach (16, 17). Midline (18 cases) and subcostal (5 case) abdominal incision was used to exposure to many other organs. Midline incision offers the advantages of being well known to all surgeons and allowing for bilateral exploration. However, it does lend itself to longer convalescence and a higher rate of ileus, and it may be difficult with obese patients. In this way, bilateral subcostal surgical incision (3 cases) was used in cases of high BMI (18, 19). 3 (10%) patient showed postoperative grade II complications, according to Clavien-Dindo classification (post-operative anemia treated with blood transfusions) (20). Invasive tumors to the sur-

TABLE 2 - INDICATION FOR LAPAROTOMIC ADRENALECTOMY.

6 PATIENTS	**Size 15,1±2,75**
20 PATIENTS	**Size 5,4±3,5** ***Imaging features concerning for malignancy:*** - Growth in size >1 cm on serial imaging (within 1 year) - Heterogeneous Poorly defined margins - Irregular shape - Necrosis - Heterogeneous - Hounsfield unit >10 on non contrasted imaging

rounding tissue or adrenal and caval veins represent an absolute contraindication to laparoscopy (1, 2, 21). So open approach is recommended in any kind of ACC because of either possible removal of adjacent structures for complete resection, and an increased risk of local recurrence with minimally invasive approach. In our study 3 right nephrectomy was necessary to remove the entire tumor mass (22). It may be difficult to identify preoperatively lesions as an adrenal malignant tumor, but its size is proportional to the risk of treating a malignant lesion (the median size is more than 11 cm). According to the National Institute of Health (NIH), incidence of adrenal carcinoma experiences a 2%-increase in case of tumors whose diameter is smaller than 40 mm, a 6%-increase in case of tumors, whose diameter is included between 41 and 60 mm and up to a 25%-increase in case of tumors with a diameter larger than 60 mm (23, 24). At present, the accepted criteria for malignancy are distant metastases or local invasion. So, in order to differentiate between benign and malignant lesions, a correct imaging evaluation is essential, above all for size and radiological appearance. Computed tomography (CT) and magnetic resonance (MRI) are the gold standard to identify resectability and relationship to other structures. A benign adrenal lesion is identified by unenhanced computed tomographic scan with a threshold of ≤10 Hounsfield units (HU). While the malignant characters are: size > 6 cm; growth in size > 1 cm on serial imaging (within 1 year); irregular shape; heterogeneous density; poorly defined margins; necrosis; Hounsfield unit > 10 with a non-contrast imaging method; < 60 % washout rate on CT imaging; hyperintensities on MRI T2-weighted imaging. Moreover, a chest computed tomographic scan is required in case of suspected adrenal carcinoma for pulmonary metastases before surgery (23, 25, 26).

Conclusions

In conclusion, our retrospective study points out the role of open adrenalectomy as the treatment of choice in selected cases with known or suspected malignant adrenal tumors and with size greater than 12 cm.

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