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Review

Surgical treatment of potentially primary malignant adrenal tumors: an unresolved issue

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ABSTRACT

Although the great majority of incidentalomas are adrenocortical adenomas, a number of them, depending on the size and radiological characteristics of the lesions, will turn out to be carcinomas. These tumors may present as suspicious on initial evaluation and potentially malignant or malignant on histology. Adrenocortical carcinoma is a rare and aggressive malignancy with evolving diagnostic and therapeutic approaches. Laparoscopic surgery has become the gold standard for surgery of benign adrenal tumors. Despite the extensive experience gained in laparoscopic adrenalectomy, controversy still remains in the management of adrenal tumors with high suspicion or evidence of malignancy. The aim of this review is to update the existing information regarding the diagnostic approach and surgical management of suspicious and potentially malignant primary adrenal tumors. The interpretation of radiologic characteristics is a cornerstone in pre-operative assessment of large adrenal masses, since open surgery remains the preferred procedure when malignancy is suspected in large tumors with possible local invasion. Despite the improvement of imaging techniques, they lack sufficient accuracy to exclude primary malignancy in tumors from 4 cm to 10 cm in size. An initial laparoscopic approach can be used in this group of patients, but early conversion to open technique is mandatory if curative resection cannot be performed. Adrenal tumors >10 cm of malignant potential should be treated by the open approach from the start. Solitary adrenal metastasis from another primary malignancy is usually amenable to laparoscopic surgery. Patients with suspected adrenal cancer should be referred to tertiary centers that perform laparoscopic and open adrenal surgery with minimal morbidity and mortality.

Key words: Adrenal carcinoma, Laparoscopic adrenalectomy, Potentially malignant, Treatment

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INTRODUCTION

Over the last few decades, the widespread application of abdominal computed tomography (CT) has revealed an increasing prevalence of clinically

inapparent adrenal masses that are detected after imaging studies conducted for reasons other than the evaluation of the adrenal glands.[1,2] The prevalence of these so-called 'incidentally' detected adrenal lesions (incidentalomas) varies from 3 to 10% depending on the methodology used in different studies, exhibiting a mean prevalence of at least 3% in persons over the age of 50 years.[1,3] Although the great majority of such lesions are adrenocortical adenomas, a number, depending on the size and radiological characteristics of the lesions, will turn out to be carcinomas.[4] These tumors may present as suspicious and potentially malignant on initial approach but are proven to be malignant, or potentially malignant, on histology. Adrenocortical carcinoma (ACC) is a rare and aggressive malignancy today benefiting from evolving diagnostic and therapeutic approaches. Currently, anatomical and functional imaging modalities, either computerized tomography (CT) or magnetic resonance imaging (MRI), comprise powerful diagnostic tools as they can distinguish with high diagnostic accuracy benign from suspicious or definitely malignant lesions.

Laparoscopic surgery has become the gold standard for surgery of benign adrenal tumors. Compared with the traditional open resection, laparoscopic adrenalectomy involves decreased requirement for postoperative analgesia, shorter hospital stay, better patient satisfaction and earlier return to normal diet and activities.[5,6] Because of the aforementioned clear advantages of laparoscopic adrenalectomy, no prospective randomized controlled trials have been undertaken comparing the laparoscopic technique with the classical 'open' technique.[7] Despite the substantial experience gained in laparoscopic adrenalectomy, controversy still remains in the management of adrenal tumors suspicious for malignancy.

The aim of this review is to update current knowledge regarding the optimal diagnostic approach, histopathological features and surgical management of suspicious and potentially malignant primary adrenal tumors.

CLINICAL PRESENTATION AND DIAGNOSTIC EVALUATION

An increasing number of ACCs are identified as incidentalomas during abdominal imaging.[2,8] Patients with adrenal tumors suspicious for malignancy are usually asymptomatic without evidence of hormonal secretion, in contrast to patients with ACC who usually present with symptoms owing to hormone hypersecretion and/or manifestations of tumor growth and extension to adjacent structures. Symptoms such as abdominal distension, pain, local discomfort or even, rarely, retroperitoneal hemorrhage are commonly found in patients with ACC. The proportion of secreting tumors among ACC varies from 25 to 70%, probably owing to differences in investigational procedures and different biochemical criteria used for the definition of hormonal hypersecretion.[2,9] However, the pattern of hormonal secretion could be strongly indicative of malignancy. In contrast to benign adrenocortical tumors that usually secrete a single class of adrenal steroids, ACC can secrete various types of steroids such as glucocorticoids, sex steroids, mineralocorticoids and/or steroid precursors such as deoxycorticosterone and compound S.[2,9] Nevertheless, although this is true in the vast majority of cases, Markou et al have reported the case of a benign adrenocortical adenoma with triple secretion of cortisol, androgens and aldosterone.[10] Co-secretion of cortisol and androgens is the most frequent hormonal manifestation in ACC, with cortisol oversecretion (alone or in combination with androgens) being present in approximately 85% of patients with functioning ACC.[11]

The European Network for the Study of Adrenal Tumors (ENSAT) recommends a comprehensive diagnostic hormonal evaluation in all patients with suspected or confirmed ACC (Table 1). Table 2 presents the revised staging system for ACC developed by ENSAT.

RADIOLOGICAL ASSESSMENT

Imaging is an essential step for the diagnosis of the malignancy of an adrenal mass.[12] Both size and appearance of the adrenal mass on CT, MRI and more recently 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) are used to distinguish between benign and malignant disease. The size of the adrenal mass, as measured by CT or MRI, remains one of the best indicators of malignancy.[13] According to the NIH consensus conference, tumors larger than 6 cm in size are highly suspicious for malignancy;[1,14]

Table 1. Recommendations of the diagnostic work-up in patients with suspected or proven ACC (ENSAT 2005, www.ensat.org/acc.htm)

Hormonal evaluation	
Glucocorticoid excess (minimum 3 out of 4 tests)	Dexamethasone suppression test (1mg, 23:00 h)
	Excretion of free urinary cortisol (24h urine)
	Basal cortisol (serum)
	Basal ACTH (plasma)
Sexual steroids and steroid precursors	DHEA-S (serum)
	17-OH-progesterone (serum)
	Androstenedione (serum)
	Testosterone (serum)
	17-beta-estradiol (serum, only in men and postmenopausal women)
Mineralocorticoid excess	Potassium (serum)
	Aldosterone/renin ratio (only in patients with arterial hypertension and/or hypokalemia)
Exclusion of a phaechromocytoma	Catecholamine or metanephrine excretion (24h urine)
	Meta- and normetanephrines (plasma)
Imaging studies	
	CT or MRI of abdomen and CT thorax
	Bone scintigraphy (when suspecting skeletal metastases)
	FDG-PET (optional)
Follow-up	
	CT or MRI of abdomen and CT thorax every 2-3 months (depending on treatment)

Table 2. Staging classification system for ACC by ENSAT

Stage	Characteristics
Stage 1	T≤5cm, N0, M0
Stage 2	T>5cm, N0, M0
Stage 3	T confined to within the adrenal gland, N1, M0
	T extending beyond limits of adrenal capsule, N0-1, M0
Stage 4	M1, any T or N

cut-off points for sizes less than 2-4 cm in size have lower predictive value.[15] In a retrospective review of 299 adrenalectomies Hamrahian et al. found that even a threshold of 2 cm is not 100% specific in ruling out malignancy using surgical histopathology as the gold standard.[16] Therefore, a tumor size of greater than 6 cm was regarded as a reasonable threshold for surgical resection, once radiologic characteristics are taken into account.[16,17] In a double-cohort study comparing tumor size of benign and malignant adrenocortical tumors, the specificity and sensitivity in predicting malignancy were 52% and 96%, respectively, for tumors 4 cm or above, 80% and 90% for tumors 6 cm or larger, 95% and 77% for tumors 8 cm or larger and 98% and 55% for tumors 10 cm or above.[18] In a series of 202 patients with ACC, the mean tumor size was 11.3±5.2cm (range: 4-30 cm),[19] although ACCs smaller than 6 cm have been increasingly reported, making the follow-up imaging of a small adrenal tumor mandatory.[20] Thus, repeating imaging to detect early tumor growth is recommended initially after 3-12 months depending on initial tumor size.[21] CT scan may be associated with approximately 40% underestimation of adrenal tumor size compared with the actual size of the histological examination.[22] In addition to the size of the tumor, other imaging features, which, although not diagnostic are suggestive of malignancy, include non-homogeneous appearance with necrotic areas, irregular margins and the presence of calcifications.[23,24]

Measurement of Hounsfield units (HU) in an unenhanced CT is very useful in differentiating malignant from benign adrenal mass. Further workup is not warranted when the lesion has an attenuation value of less than 10 HU, suggesting a lipid-rich adrenal adenoma. A high density (>10 HU) indicating a low-fat content will make a clinician more suspicious that the lesion may be malignant, although lipid-poor adenomas represent 10-40% of all adenomas.[24] Using a threshold value of 10 HU and after analyzing 11 studies, Bolland et al reported a sensitivity and specificity of 71% and 98%, respectively.[25] However, as lipid-poor benign adenomas may have greater than 10 unenhanced HU values, it has been suggested that a 20 HU density presents an acceptable cut-off value indicative of a benign tumor in a less than 4 cm in size mass and in the absence of a history of malignancy.[17] According to Mansmann et al, thresholds of 16.5 and 18 HU attained both high sensitivity and specificity of 85-95% and 93-100%, respectively.[8]

In a very recent study, Birsen et al. proposed an algorithm for the management of patients with ad-

renal incidentalomas in which risk stratification for malignancy is based on tumor size and HU density. In a study with 157 patients, the authors suggested that an algorithm utilizing hormonal activity at the first decision step followed by a consolidated risk stratification, based on tumor size and HU density, has potential to spare a substantial number of patients from unnecessary surgery for adrenal incidentaloma.[24]

Dynamic measurements of contrast-enhanced densities provide additional information. Enhancement washout of less than 50% and a delayed attenuation value of greater than 35 HU (on 10-15 min delayed enhanced CT) strengthens the suspicion of malignancy.[26-29] MRI has effectiveness similar to CT in distinguishing benign from malignant adrenal masses.[30]

Today FDG-PET is emerging as a powerful adjuvant imaging modality in the differentiation of benign from malignant disease.[31-33] High uptake of 18F-FDG demonstrates increased glucose metabolism and indicates malignancy. Thus, FDG-PET may be highly valuable during evaluation of adrenal masses that have not been fully characterized by either CT or MRI, especially when used in combination with CT.[34] In a study of 150 patients, the combination of unenhanced and qualitative CT data with retrospective FDG-PET data yielded a sensitivity of 100%, a specificity of 99% and an accuracy of 99% for the detection of malignancy.[25] In a recent large retrospective study, Pitts et al concluded that FDG-PET is not required for adrenal mass diagnosis in most patients in contemporary practice but may be helpful in specific situations.[35]

Fine-needle biopsy of suspected ACC under CT guidance is of limited use. There are few indications of its efficacy, taking into account the benefit ratio,[36,37] and it is performed only if the lesion appears locally unresectable or other primary or metastatic disease is present.[38,39] An appropriate biochemical evaluation to exclude pheochromocytoma should always precede given that fine needle biopsy could be hazardous in this group of patients.[39]

HISTOPATHOLOGY OF POTENTIALLY MALIGNANT PHEOCHROMOCYTOMAS

Catecholamine-secreting tumors that arise from chromaffin cells of the adrenal medulla and the sympathetic ganglia are referred to as “pheochromocytomas” and “extra-adrenal catecholamine-secreting paragangliomas” (“extra-adrenal pheochromocytomas”), respectively. About 10% of all catecholamine-secreting tumors are malignant, although recent studies suggest that this figure is probably an underestimate.[40-42] Malignant pheochromocytomas are histologically indistinguishable from benign and only the presence of local invasion or distant metastases determine the presence of a malignant pheochromocytoma which may occur as long as 20 years after resection.[42-44]

In 2002, Thompson developed the Pheochromocytoma of the adrenal gland scaled score (PASS). This score on histological features as malignant pheochromocytomas more frequently demonstrated invasion (vascular [score = 1], capsular [score = 1], periadrenal adipose tissue [score = 2]), large nests or diffuse growth (score = 2), focal or confluent necrosis (score = 2), high cellularity (score = 2), tumor cell spindling (score = 2), cellular monotony (score = 2), increased mitotic figures (>3/10 high power fields; score = 2), atypical mitotic figures (score = 2), profound nuclear pleomorphism (score = 1), and hyperchromasia (score = 1) than the benign tumors. It was suggested that the PASS weighted for these specific histologic features can be used to separate tumors with a potential for a biologically aggressive behavior (PASS > or =4) from tumors that behave in a benign fashion (PASS <4). Furthermore, the author stated that a combined score of ≥4 in no way guarantees the development of metastatic disease. Similarly, a combined score of ≤3 does not guarantee that a patient will not develop metastatic disease at some point in the future.[45]

PASS reliability has been evaluated by several studies, with conflicting results. Most studies have indicated that PASS can be used for the diagnosis of malignant pheochromocytomas,[46-48] while other authors have suggested that PASS requires further refinement and validation before it can be used for clinical prognostication.[49,50]

Another factor that suggests a malignant course is large tumor size and weight.[47] It has been hypothesized that any adrenal pheochromocytomas >6cm (or >5cm in some series) should be viewed suspiciously.[42] August et al have suggested that metastasized and nonmetastasized pheochromocytomas can be eas-

ily distinguished on the grounds of tumor weight.[51] Other authors have found that although malignant tumors are larger than benign ones, there are no cut-off values that could differentiate between benign and malignant tumors.[45,48] Agarwal et al on the other hand have suggested that presently there is not enough evidence to indict a large (>6 cm) pheochromocytoma as malignant.[50]

The Ki-67 proliferative index is considered to be of great usefulness in predicting the malignant potential of pheochromocytomas. This antigen, found throughout the cell cycle and absent in resting cells, thus constitutes a powerful tool to assess tumoral growth rate. However, its relatively high specificity is related to low sensitivity, as almost half of malignant pheochromocytomas show a Ki-67 index <2-3%. Therefore, many authors have had to choose a very low Ki-67% cut-off value such as 2 or 2.5% in order to be able to separate malignant from benign tumors.[47,48,51,52] Despite all these limitations, Ki-67% staining can be helpful by prompting the pathologist to look carefully for significant histologic predictors of malignancy.

Several immunohistochemical markers have been studied as potential predictors of the biologic behavior of pheochromocytomas. Absent or weak inhibin/activin beta-B subunit,[53] pS100 expression[45,47] and nm-23 expression[54] and on the other hand overexpression of topoisomerase II alpha, MIB-1, galectin-3[54] and Cyclooxygenase-2[54-57] necessitate a close histopathological evaluation and follow-up, as the risk of malignancy and recurrence is high in tumors that express these markers. Similarly, patients with succinate dehydrogenase B mutations are more likely to develop malignant disease.[58-60] The immunohistochemical expression of p53, Bcl-2, mdm-2, cyclin D1, p21, p27, p53, E-cadherin and HER-2/neu did not prove to be useful in the prediction of the biologic behavior of adrenal and extra-adrenal pheochromocytomas.[48,55]

Kimura et al developed a scoring scale based on six factors: histological pattern, cellularity, coagulation necrosis, vascular/capsular invasion, Ki-67 and types of catecholamine produced, while they also classified tumors into well differentiated, moderately differentiated and poorly differentiated types.[54]

HISTOPATHOLOGY OF POTENTIALLY MALIGNANT ADRENOCORTICAL TUMORS

Preoperative diagnosis of malignancy in adrenocortical neoplasms is feasible only in the presence of metastases or invasion into surrounding tissues. Prediction of malignancy requires reliable objective clinical, biochemical and pathologic (morphologic and molecular) markers, which are currently unavailable.[61]

Weiss proposed that the presence of three or more of the following nine criteria highly correlates with subsequent malignant behavior: nuclear grade III or IV; mitotic rate greater than 5/50 high-power fields; atypical mitoses; clear cells comprising 25% or less of the tumor; a diffuse architecture; necrosis; and invasion of venous, sinusoidal, and capsular structures.[62]

In the literature, mention is usually made of the WHO classification along with, in pathological reports, the Weiss criteria, as well as data according to Van Slooten and Hough. Morphological features that have been used as predictors of malignancy are tumor weight and size, mitotic activity, necrosis, lymphovascular invasion, capsular invasion and hemorrhage.[63-66]

Another useful method to predict the potential biological activity of large adrenocortical tumors is the aneuploid pattern in DNA flow cytometry.[67,68] Nevertheless, the reliability of aneuploidy in predicting survival, response to therapy or hormone secretion has been questioned, thus limiting its use.[69]

The immunohistochemical expression of several markers has been studied in adrenocortical tumors in an attempt to identify reliable objective predictors of malignancy. Gupta et al found that immunohistochemical staining for Topoisomerase IIα, MIB-1, p53 and the retinoblastoma gene protein product is helpful in the recognition of neoplasms with aggressive behavior, while E-cadherin and HER-2/neu do not serve as useful markers.[55]

Detection of telomerase activity, an enzyme that contributes to maintaining telomere length, might also be a valuable tool for predicting the malignant potential of adrenal tumors.[70]

TREATMENT OF POTENTIALLY MALIGNANT ADRENAL TUMORS

In the era of advanced laparoscopic surgery, lapa-

roscopic adrenalectomy has gained popularity and several institutions have expanded the indications for this procedure. Potentially malignant primary adrenal tumors and solitary adrenal metastases, once considered contraindications for the laparoscopic approach, are currently being removed laparoscopically in several institutions.[71-75] Given that no reliable and accurate preoperative diagnostic test to confirm the diagnosis of primary malignant adrenal tumor or local invasion exists, it is often difficult to decide if the laparoscopic approach can achieve a curative resection.

Despite the considerable experience gained in laparoscopic adrenalectomy, controversy remains as to the management of adrenal tumors with high suspicion or evidence of malignancy. A curative laparoscopic resection incorporates the oncologic principles of the open technique such as resection of the totality of the adrenal tumor including the periadrenal adipose tissue, avoiding fracture of the tumor capsule.[76]

Laparoscopic surgery can be an accepted method in the surgical management of cancer if it fulfills a number of parameters. It is of paramount importance to have data demonstrating that the operative morbidity and mortality of laparoscopic surgery is equally safe or safer compared to conventional open operation. In addition, it should be as radical as conventional open surgery.

The role of laparoscopic surgery for malignant or potentially malignant adrenal tumors is controversial because there are few series in the literature on this relatively rare disease (Table 3). Furthermore, there have been concerns regarding local recurrences and port-site metastasis after apparently curative resections.[77] The pathogenesis of port-site metastasis remains unknown but is probably multifactorial. Direct wound implantation of tumor cells plays a major role in the development of port-site metastasis. However, this does not explain the development of metastases at non-extraction port-sites. Other etiological factors are contamination of instruments, aerolization of tumor cells, the "chimney effect", poor surgical technique, improper handling of the tumor, pneumoperitoneum, the effect of carbon dioxide on tumor cells and lack of preventive measures against local recurrence and port-site metastasis.[6,78] Several strategies have been

Table 3. Series comparing open versus laparoscopic adrenalectomy for adrenocortical cancer

Author	Technique	No. of patients	Recurrence rate, %	p	Overall survival, %	Overall survival, months	p
Gonzalez et al, 2005[105]	OA	133	86			43	
	LA	6	100			15	
Adler et al, 2007[105]	OA	8	0		54	17	0.96
	LA	11	0		34	19	
Porpiglia et al, 2010[106]	OA	25	64				
	LA	18	50				
Brix et al, 2010[107]	OA	117	61	0.56		32	0.02
	LA	35	54			64	
Miller et al, 2012[92]	OA	71	63*			103.1/43.7 (stage II/III)	0.002 /0.77 (stage II/III)
	LA	17	69*			50.9/27.5 (stage II/III)	
Mir et al, 2013[96]	OA	26	27*	0.099	60*		0.122
	LA	18	22*		39*		
Cooper et al, 2013[93]	OA	256	80	0.001		46*	0.070
	LA	46	76.1			53.5*	
Donatini et al, 2014[100]	OA	21	24	0.655		85	
	LA	13	31			81	

OA open adrenalectomy, LA laparoscopic adrenalectomy. *Adjustment for stage resulted in statistically significant differences.

proposed to prevent port-site metastasis. In order to achieve better results, strictly oncologic techniques should be followed, as in open surgery. Moreover, additional techniques such as wound protectors, evacuation of the pneumoperitoneum through port and peritoneal wound closure have been proposed and applied successfully.[79-82]

Three cases of diffuse peritoneal dissemination and death of patients who underwent laparoscopic adrenalectomy for adrenal cancer have been reported in a study.[82] Further, in a study of 13 patients (six with ACC and seven with metastasis), the mean size of the malignant lesions was 5.9 cm and, during a mean follow-up of 30 months, three patients died, one of whom had intraperitoneal and trocar port-site seeding.[83] In another study, 31 patients underwent a total of 33 laparoscopic adrenalectomies, 26 for metastatic cancer and 7 for primary adrenal malignancy. During a follow-up period of 26 months 15 patients died and 7 developed a local recurrence; however, there was no port-site metastasis and overall 5-year survival reached 40%.[84]

Potentially malignant pheochromocytomas and adrenocortical tumors must be approached cautiously. The possibility of tumor fragmentation and abdominal dissemination is significant. The surgeon must mobilize the tumor and surrounding adipose tissue without grasping the tumor or gland. The ultrasonically activated scalpel should be used carefully so that it does not traumatize the tumor surface or adrenal tissue and thus create fragmentation and malignant cell dissemination.[6]

The role of the laparoscopic approach for large tumors is also still controversial. Tumor size is a good index but cannot be used as an absolute predictor of malignancy.[74] It has been estimated that the risk for cancer in adrenal tumors larger than 6 cm is 1/60 adrenalectomies performed, i.e. 1.67%.[85] On the other hand, 13.5% of ACC were diagnosed in patients with adrenal tumors smaller than 5 cm.[86] There are not many cases reported about patients with malignancies more than 8 cm in size; however, a review of the literature shows that these patients may still undergo laparoscopic surgery.[87-90] Overall morbidity and mortality is independent of the size of tumor and the mean operative time is not significantly different.[91] Conversion to open surgery is more often performed in larger tumors due to invasion of adjacent tissues or organs or due to capsular disruption. Benign lesion sizes of 12 cm to 14 cm have been cited as the upper limit for laparoscopic adrenalectomy in most of the studies.[88] The hand-assisted laparoscopic approach has been proposed as a good alternative to open conversion if a difficult dissection is encountered intraoperatively.[87]

CURRENT DATA AND TRENDS

Several studies point to the better oncologic results achieved via the open approach following resection for ACC.[92-96]

Advances in imaging and biochemical evaluation should establish theoretically the diagnosis of primary adrenal malignancy in the majority of cases with suspicious adrenal neoplasms, the aforementioned holding true in clinical practice with regard to tumors larger than 10 cm. On the other hand, there are still large numbers of patients with non-secreting tumors measuring 4-10 cm who present preoperative diagnostic dilemmas. On this basis, this particular group of patients merits particular attention.

The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) recommends that "if a laparoscopic approach is chosen due to diagnostic ambiguity, conversion to open surgery is strongly recommended".[97] This recommendation is obviously suitable for all large adrenal masses with involvement of adjacent structures and/or regional lymph node infiltration[98]

However, based on increased laparoscopic expertise, the positional statement of the European Society of Endocrine Surgeons (ESES) on primary malignant tumors included a modification in the international trend: "Laparoscopic resection of ACC/potentially malignant tumors, which includes removal of surrounding periadrenal fat and results in an R0 resection without tumor capsule rupture, may be performed for pre- and intra-operative stage 1-2 ACC and tumors with a diameter less than10 cm (level of evidence C)".[76]

Similar suggestions have been recorded in the literature from several institutions.[99-103] The cut-off size of 10 cm in adrenal masses was considered as

the upper limit for laparoscopic resection of tumors suspicious for malignancy.[78,100] Conversely, the results of a recent retrospective study challenged the trend of the laparoscopic approach for malignant or possible malignant tumors with a diameter less than 10 cm.[92] Miller et al. reported increased incidence of local recurrence after laparoscopic surgery and improved survival in patients undergoing open adrenalectomy for primary adrenal malignancy. Their results are also in accordance with a recent study conducted by a large referral center.[93] Nevertheless, it should be noted that most laparoscopic resections for malignancy had been performed with no clear-cut or uncertain selection criteria and with various levels of laparoscopic expertise. Moreover, a recent study comparing open vs laparoscopic adrenalectomy for adrenal metastases concluded that only patients with tumors larger than 7.5 cm may benefit from an open surgical approach.[104]

Cautious patient selection and intraoperative oncologic principles are mandatory to achieve reliable results in the use of laparoscopic surgery for malignant adrenal tumors. Extensive international and personal experience indicates that laparoscopic resection is feasible and safe for tumors less than 10 cm, without periadrenal infiltration. The transabdominal laparoscopic approach is ideal for vascular exposure, clear mobilization of the periadrenal adipose tissue including the intact tumor and identification of lymphadenopathy.

CONCLUSIONS

The interpretation of radiologic characteristics is a cornerstone in pre-operative assessment of large and/or suspicious adrenal masses, since open surgery remains the preferred procedure when malignancy is suspected in large tumors. Despite the improvement of imaging techniques, they lack sufficient accuracy to exclude primary malignancy in tumors that are from 4 to 10 cm in size. The initial laparoscopic approach can be used in this group of patients, while early conversion to the open technique is mandatory if curative resection cannot be performed. Primary adrenal tumors >10 cm that are of malignant potential should be treated by the open approach from the start. Solitary adrenal metastases from another primary malignancy are usually amenable to laparoscopic surgery. Patients with suspected adrenal cancer must be referred to tertiary centers that perform laparoscopic and open adrenal surgery with minimal morbidity and mortality.

CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest and that they received no specific funding for this article.

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