ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 6 | Issue: 7 | July 2020 || Journal DOI: 10.36713/epra2013 || SJIF Impact Factor: 7.032 ||ISI Value: 1.188

ADRENAL INCIDENTALOMA-A REVIEW

Luis Armando López-Rico
General surgery department.
Hospital General de Zona 5.
IMSS. Sonora,
Mexico.

Carlos Enrique Luna-Guerrero
General surgery department.
Hospital General de Zona 5.
IMSS. Sonora,
Mexico.

José Victor Pérez-Navarro
General surgery Department.
Centro Médico de Occidente.
IMSS. Guadalajara,
Mexico.

Iván Rodolfo Martínez-García
General surgery department.
Hospital General de Zona 5.
IMSS. Sonora,
Mexico.

Edgar Vargas-Flores
Hospital General Dr. Manuel Gea González.
Mexico City,
Mexico.

ABSTRACT

Adrenal incidentalomas occur asymptomatically in up to 80% of cases, but is generally accompanied by comorbidities such as type 2 diabetes mellitus and hypertension. Every patient diagnosed with an adrenal incidentaloma should be evaluated with a detailed medical history and thorough physical examination. Laparoscopic adrenalectomy is currently the gold standard in the management of this pathology either by transabdominal approach or by retroperitoneoscopy. Advances in technology have made it possible for robot adrenalectomy to be performed safely today, but the role it plays in the field of cost-benefit has not yet been clearly defined. The open approach is reserved for those cases where an adrenocortical carcinoma is suspected.

INTRODUCTION

An adrenal incidentaloma is defined as any tumor larger than one centimeter which is diagnosed in an imaging study indicated for a different cause. The incidence varies with age, occurring in less than 1% of those under 30 years of age and up to 7% in those over 70 years of age. This occurs asymptomatically in up to 80% of cases, but is generally accompanied by comorbidities such as type 2 diabetes mellitus and hypertension. Every patient diagnosed with an adrenal incidentaloma should be evaluated with a detailed medical history and thorough physical examination. The potential for malignancy of these lesions must be determined by means of imaging studies, currently there are three main imaging techniques that are used for this purpose: computed tomography (CT scan), magnetic resonance imaging (MRI) and positron emission tomography with F-2-desoxy-D-glucose (FDG-PET/CT). The functional state of the adenomas must also be determined with a biochemical evaluation since the symptoms that most patients present will be due to the overproduction of adrenal hormones, this translating into the need to take the patient to a surgical intervention, evaluating each case individually and taking into account the patient's current state of health, his pre-operative risk, his comorbidities and the patient's preference. Laparoscopic adrenalectomy is currently the gold standard in the management of this

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 6 | Issue: 7 | July 2020 || Journal DOI: 10.36713/epra2013 || SJIF Impact Factor: 7.032 ||ISI Value: 1.188

pathology either by transabdominal approach or by retroperitoneoscopy. Advances in technology have made it possible for robot adrenalectomy to be performed safely today, but the role it plays in the field of cost-benefit has not yet been clearly defined. The open approach is reserved for those cases where an adrenocortical carcinoma is suspected .

DEFINITION

The adrenal incidentaloma is defined as a mass greater than 1 cm that is diagnosed incidentally, in an imaging study by an indication other than the adrenal disease itself and which generally presents asymptomatic or subclinical.[1] The term incidentaloma is defined by very restrictive criteria, however, frequently in the medical literature this term is used more broadly to refer to any tumor dependent on the adrenal gland.

EPIDEMIOLOGY

A report based on 87,065 autopsies showed a frequency of adrenal adenomas of up to 6% of the general population. Having an increase in prevalence with age, being present in less than 1% of patients younger than 30 years and up to 7% of patients older than 70 years. Similar results have been found in studies based on abdominal tomography, reporting an incidence of up to 4% in the general population.[2]

Non-functional adenoma is the most frequently found diagnosis in cases of adrenal incidentaloma (up to 80% of cases), the incidence of other diseases varies in different types of studies, the incidence of pheochromocytoma ranges from 1.5% to 23% and for adrenocortical carcinoma it varies from 1.2% to 12%.[3]

CLINICAL EVALUATION

A detailed clinical evaluation and a thorough physical examination are of superlative importance since up to 30% of patients with an adrenal incidentaloma may harbor excessive cortisol , catecholamines, or aldosterone production depending on the criteria used to define excess production.[3] That is why the clinical history should be aimed at discovering manifestations of hypercortisolemia , primary aldosteronism, excess of catecholamines, hyperandrogenism and abdominal discomfort. A history of paroxysmal hypertension, fluctuations in blood pressure during anesthesia, syncope events should alert to the possibility of a pheochromocytom.[3]

Different types of cancer have the ability to metastasize to the adrenal gland including lung, breast, kidney, melanoma, so a history of malignancy and weight loss should alert us to this possibility.[2]

A combination of characteristics that reflect excess androgens and cortisol should warn of the possibility of a cortical carcinoma since this can present in up to 1.2% of cases in the form of an adrenal incidentaloma .[3]

Family history should be ascertained by components of multiple endocrine neoplasia, Von Hippel-Lindau syndrome and neurofibromatosis type 1, although family syndromes are regularly rare, they are especially important in bilateral lesions and subclinical pheochromocytomas .[4]

The initial evaluation in these patients should be aimed at determining two important characteristics: the potential for malignancy of the adrenal tumor, the functional status and its magnitude in the patient's clinical presentation, since this translates into indications for surgical treatment for these patients.

DETERMINATION OF THE POTENTIAL OF MALIGNANCY

All patients with a recent diagnosis of incidentaloma should be evaluated with imaging studies that help to identify characteristics that are commonly attributed to lesions of benign origin, generally less than 4 centimeters in size, well-defined contours, without invasion of neighboring structures and density homogeneous to the application of contrast. Benign adrenal adenomas contain large amounts of intracytoplasmic lipids, approximately 70% of adrenal adenomas are rich in lipids.[9] For the differentiation of malignant from benign lesions, there are three imaging techniques that are mainly used today: computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography with F-2-deoxy-D-glucose (FDG-PET / CT).

Computed tomography: Non-contrast CT scan of the abdomen has become the standard for the initial evaluation of adrenal incidentalomas. The European Society of Medical Endocrinologists in its 2017 Clinical Practice Guideline recommends that if a homogeneous lesion is found in the initial evaluation of an incidentaloma of less than 4 cm and with an attenuation coefficient of less than 10 HU this type of lesion requires no further imaging studies.

Contrast enhanced Computed tomography: Up to 30% of adrenal lesions have random pattern by non-contrast tomography (10-30 HU) for which is indicated a contrasted tomography with late washouts (delay washouts).[6]

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 6 | Issue: 7 | July 2020 || Journal DOI: 10.36713/epra2013 || SJIF Impact Factor: 7.032 ||ISI Value: 1.188

Magnetic resonance imaging: Adenomas with high lipid content usually lose the intensity of the lesion in out-of-phase images compared to in-phase images, while malignant lesions and pheochromocytomas (but also low lipid adenomas) remain unchanged. The simple analysis of the loss of intensity during the phases can be diagnosed in most cases, in those indeterminate cases quantitative analyzes such as the adrenal-spleen signal ratio can be used. However, there is a significant overlap in the characteristics of malignant and benign lesions. Therefore, in some cases MRI cannot distinguish between malignant and benign lesions.[11]

F-FDG-PET: It is a modality of nuclear medicine, through which tomographic images are obtained after injection of the radio marker (18-Fluor) used to mark 2-deoxy-D-glucose (18-F-FDG). Glucose and deoxyglucose enter the cell via cellular glucose transporters and are phosphorilyzed, but while glucose is enzymatically decomposed, deoxyglucose is stored in intracellular compartments, malignant cells have an increase in glucose requirements and therefore have a higher consumption than normal cells. Quantitative measurements of the 18-F concentration within tissues is the most commonly used clinical index. The standard consumption value (SCV) compares the intensity of 18-F consumption within the adrenal gland with an average intake of the body, this technique has a sensitivity of 99 - 100% and a specificity of 94 - 100%, with a positive predictive value of 83% for malignant lesions.[2]

Role of Fine Needle Aspiration Biopsy: The use of aspiration biopsy has decreased as a result of improving the accuracy of diagnostic imaging and its use is not routinely indicated at present in the diagnostic approach to this pathology.[1] However, it may still be useful in patients diagnosed with an adrenal mass in a patient with a history of an extra adrenal malignancy as long as the following three criteria are met:

- The lesion is shown to be hormonally inactive (in particular, pheochromocytoma has to be excluded).
- The lesion has not been characterized as benign by image.
- The treatment could have a significant change depending on the result of the biopsy

As for the diagnostic performance, it is known that the aspiration biopsy has a sensitivity and specificity of 87% and 100% respectively. The rate of non-diagnostic biopsies is around 11.2%, while the rate of complications is 2.5%.[7] Although rare, complications that can occur are pneumothorax, bleeding, infection, and pancreatitis.

Biochemical evaluation

Up to 30% of patients with an adrenal incidentaloma may harbor excess cortisol, catecholamines, or aldosterone production depending on the criteria used to define excess production.

Autonomous cortisol secretion: Defined as the subtle autonomous production of cortisol by an adrenal mass or incidentaloma, which is associated with suppression of production by the contralateral gland, but without obvious clinical signs of Cushing's syndrome , a prevalence of up to 20% in patients with an incidentaloma .

The use of the low-dose suppression test for dexamethasone is recommended for screening with a sensitivity and specificity of 73-100% and 90% respectively.[5] Levels of blood of cortisol after the administration of 1 mg dexamethasone ≤ 50 nmol / L (≤1.8 µg/dL) is a diagnostic criterion for exclusion of autonomous secretion of cortisol, level of cortisol serum between 51 and 138 nmol/L (1.8-5.0 µg/dL) are taken as evidence of possible autonomous secretion of cortisol, whereas serum levels above 138 nmol/L (5.0 µg/dL) confirm autonomous secretion cortisol.[1]

Diagnosis

Screening

Measurement of plasma aldosterone concentrations (PAC) and plasma renin activity (PRA) or direct renin concentration for analysis of the aldosterone-renin ratio (ARR), is currently the most reliable method of screening for primary aldosteronism.[8] To adequately perform this test, it is recommended that all medications that interfere with the renin- angiotensin system (antihypertensives including diuretics) be discontinued 4 weeks prior to sample collection. Other medications that should be withdrawn, but with a shorter period of two weeks are beta-blockers, clonidine, methyldopa, NSAIDs, ACEIs , angiotensin receptor blockers, and dihydropyridine calcium channel blockers .

Confirmatory

Suppression tests used most commonly used are salt loading (via intra venous or oral) fludrocortisone, or challenge with captopril. The salt load test is widely used as it is accessible, cheap and reliable, but there is a risk of water overload. 2L of 0.9% saline are administered for 4 hours and thereafter the PAC is measured. This has a sensitivity of 88% using a cut-off

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 6 | Issue: 7 | July 2020 || Journal DOI: 10.36713/epra2013 || SJIF Impact Factor: 7.032 ||ISI Value: 1.188

value of ≤5 ng/dL (≤139 pmol/L), the suppression test consists of administering 25-50 mg of captopril orally after sitting or standing. The reference cutoff is a decrease in PAC ≤ 30% or an ARR ≥ 200 pg / mL.[9]

TREATMENT

The presence of symptoms or tumors that are biochemically functional are an indication for surgical treatment in adrenal masses. In asymptomatic masses, several clinical, radiological, biochemical and histological factors must be taken into account that help to distinguish tumors with malignant potential from benign tumors, determining which can be observed and which should undergo surgical treatment. An issue that is still controversial is the autonomous secretion of cortisol or also known as sub clinical Cushing's syndrome .

Peri-operative treatment:

All patients diagnosed with an adrenal incidentaloma, who will be taken to surgical treatment, and especially those with a functioning hormonal status, should be treated in a multidisciplinary team with experience in managing this type of disease in the pre-operative, the trans- operative and the post-operative since each of these has peculiarities in its management.

Surgical approach
Trans- abdominal laparoscopic adrenalectomy vs posterior retroperitoneoscopy adrenalectomy

Currently, laparoscopic adrenalectomy is the gold standard in the treatment of this pathology, either by trans- abdominal approach or a retroperitoneoscopy approach, both offer advantages and disadvantages that will be discussed later. The trans-abdominal approach was initially widely accepted since the vision it offers is more familiar to most surgeons and allows it to be combined with other abdominal procedures. This approach requires mobilization of the colon, spleen, pancreas (left) and liver (right) and lysis of adhesions if they are present from previous surgical procedures. Laparoscopic adrenalectomy by anterior approach has been shown to be possible safely without a significant increase in surgical time, rate of complications, and rate of conversion or in the days of hospital stay.[10]

The retroperitoneal approach offers direct access to the gland without requiring the mobilization of other organs or the release of previous adhesions. For the selection of the type of approach, it is always imperative to take into account the preference of the surgeon, considering the approach with which he is most familiar, some authors suggest the choice of the type of approach based on anthropometric measurements of the patient. They recommend a retroperitoneal approach in patients with a distance from the fascia of Gerota the lower skin 5 cm and if the twelfth rib is rostral or level of the hilum kidney. The trans-abdominal approach in obese patients with a body mass index greater than 30 a distance from Gerota to the skin greater than 5 cm, and in cases of tumors larger than 6 cm.[11]

Numerous studies have compared the surgical results of trans-abdominal laparoscopic adrenalectomy (TALA) and posterior retroperitoneoscopy (PRP). However, the results are still contradictory. Some authors have reported PRP is superior to the TALA in surgical time, bleeding, post-surgical pain and days of hospital stay.[12,13,14] Other studies have reported no difference between these two approaches in surgical outcomes including surgical time,[15,16,18] bleeding[17,18] and hospital stay.[15,18]

Surgical Technique:
Trans abdominal laparoscopic adrenalectomy

The patient is placed in lateral decubitus with the affected side up, the arm is raised and placed on a support, pillows are placed between the legs with the lower leg flexed and the upper leg straight, the upper anterior iliac spine is placed on the break point of the table and this is folded to increase the surgical site, the skin is prepared and the patient is dressed regularly, with a sterile skin marker the costal margin and midline are marked, the entry port is performed at the level of the anterior axillary line 2 cm below the costal margin, using the Veress needle or Hasson technique, the abdominal cavity is inflated at 12 to 15 mmHg and a diagnostic laparoscopy is performed, two other work ports are placed 5 mm lateral to the initial port with a minimum of 5 cm between them to allow adequate mobility.[2]

Surgery begins by incising at the level of the right triangular ligament and bringing this dissection to the level of the diaphragm with bipolar energy or with an ultrasonic dissector. Once the liver is released, it is mobilized towards the midline, allowing visualization of the inferior vena cava (IVC) and the adrenal gland, a plane is made between the IVC and the medial edge of the gland with blunt dissection. Delineate the adrenal vein which drains directly into the IVC and double ligation with clips, and cut with a vascular cartridge, once the adrenal vein is secured the rest of its medial-inferior and posterior ligaments are dissected, it is important to maintain gentle traction to avoid capsule rupture. Once the gland is released it is placed in a recovery bag and removed through the 12mm port.[19]

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 6 | Issue: 7 | July 2020 || Journal DOI: 10.36713/epra2013 || SJIF Impact Factor: 7.032 ||ISI Value: 1.188

Surgical technique: posterior retroperitoneoscopy adrenalectomy

The patient is placed in the prone position, jack-knife position. The marks to be taken into account in this position are the 12th rib and the iliac crest. The initial incision is made just below the 12th rib, sharp dissection is performed until entering the retro peritoneum. The index finger is then used to create a gap, and under direct palpation a 5-mm trocar is placed lateral to the spinous musculature. A 12-mm port is placed posteriorly through the initial incision and one more than 5-mm lateral to it. After this, the cavity is insufflated at a pressure of 20 to 24 mmHg, which allows adequate exposure. The first reference that we must identify is the upper pole of the kidney, the vena cava is identified at the medial level, the mobilization of the gland should always start at the lower edge since the dissection of this space can be performed with minimal mobilization of the gland, then the adrenal vein can be identified at the lateral edge of the gland, once dissected it is divided using a vascular stapler or with clips, once the vein is secured the other ligaments can be divided with an ultrasonic dissector. Once the gland is released, it is placed in a bag and removed, hemostasis is verified by decreasing the insufflation pressure to 12 mmHg. Once hemostasis is secured, the ports are removed and the initial incision is closed flat.[2]

Robot adrenalectomy

Advances in minimally invasive surgery are increasingly used. In 2001, the first robot adrenalectomy was reported. Since then, much information has been published comparing this with laparoscopic adrenalectomy, without showing significant differences. In 2017, a meta-analysis was published that included 27 studies, with a total of 1,162 patients undergoing adrenalectomy, of which 747 were performed with robots and 415 by laparoscopy. There were no significant differences in the rate of intra-operative complications, postoperative complications, mortality, conversion to laparotomy, bleeding or a significantly higher surgical time.[18] Robot adrenalectomy is possible and can be performed safely performed with clinical results similar to laparoscopy in the appropriate population. However, better studies with a good level of evidence should be carried out to determine the role of laparoscopic adrenalectomy in the field of cost-effectiveness in the years to come.

Open approach

Adrenocortical carcinoma (ACC) is the main threat for an adverse outcome in patients undergoing surgical treatment. In laparoscopic adrenalectomy in patients with suspected ACC, the possibility of incomplete macroscopic resection, capsule rupture, conversion to laparotomy, and invasion of peri-adrenal fat is a concern. That is why in 2015 the NCCN clinical practice guidelines recommended an open approach when suspected of adrenocortical carcinoma.[20]

However, the clinical practice guidelines of the European Society of Endocrinologists recommend the laparoscopic approach in patients with unilateral adrenal incidentaloma with suspicious findings of malignancy less than 6 centimeters, but without evidence of local invasion.[1]

Partial adrenalectomy

In the last decade there has been a growing interest in partial adrenalectomy, adrenal insufficiency following bilateral adrenalectomy results in a lifetime risk of morbidity from an Addisonian crisis (35%), decreasing the quality of life and a mortality risk of 3%.[21]

The incidence of bilateral adrenal tumors is estimated to be from 4.25 to 80%. Pheochromocytoma may be bilateral in 80% of cases while sporadic cases reach a rate of 25%, aldosterone producing adenomas are bilateral in up to 4%.[22]

Partial adrenalectomy is a procedure that can be performed safely by laparoscopy, the requirement to perform a partial adrenalectomy is to leave enough well vascularized tissue after resecting the tumor, which can be done using ultrasound energy and an intraoperative ultrasound.

Concern with this conservative cortex technique recurrence rates reach 21 to 60%. Taking the patient to life-long clinical and biochemical surveillance.

CONCLUSION

Patients with adrenal incidentaloma should get a full history and complete clinical examination. Imaging studies are helpful in most of the patients to an adequate surgical planning. Laparoscopic approach is useful to resolve most of this cases. Nevertheless, the treating surgeon should always assess the risk of potential malignancy.

REFERENCES

1. *Fassnacht M, Arlt W, Bancos I, Dralle H, Newell-Price J, Sahdev A, et al. Management of adrenal incidentalomas: European Society of Endocrinology Clinical Practice Guideline in collaboration with the European Network for the Study of Adrenal Tumors. Europe Jour Endocrinol 2016;175: G1-G34.*
2. *Carr A, Wang T. S. Minimally Invasive Adrenalectomy. Surg Oncol Clin N Am 2016; 25: 139–152.*
3. *Lee J-M, Kim M, Ko S-H, Koh J-M, Kim B-Y, Kim S. Clinical Guidelines for the Management of*

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 6 | Issue: 7 | July 2020 || Journal DOI: 10.36713/epra2013 || SJIF Impact Factor: 7.032 ||ISI Value: 1.188

Adrenal Incidentaloma. Endocrinol Metab 2017; 32:200-218

4. *Ioachimescu A, Remer E, Hamrahian A. Adrenal Incidentalomas a disease of modern technology offering opportunities for improve patient care. Endocrinol Metab Clin N Am 2015 ;44(2): 335–354.*
5. *Taffel M, Haji-Momenian S, Nikolaidis P, Miller F. Adrenal Imaging: A Comprehensive Review. Radio Clin N Am 2012; 50(2): 219–243.*
6. *Sahdev A, Willatt J, Francis IR, et al. The indeterminate adrenal lesion. Cancer Imaging 2011; 10(1):102–13.*
7. *Bancos I, Tamhane S, Shah M, Delivanis DA, Alahdab F, Arlt W, et al. The diagnostic performance of adrenal biopsy: a systematic review and meta-analysis. Eur Jour Endocrinol 2016; 175(2): R65-R80.*
8. *Arlt W, Lang K, Sitch AJ, Dietz AS, Rhayem Y, Bancos I, et al. Steroid metabolism analysis reveals prevalent glucocorticoid excess in primary aldosteronism. JCI Insight 2017; 2: 931-936.*
9. *Stowasser M, Gordon RD. Primary aldosteronism: changing definitions and new concepts of physiology and pathophysiology both inside and outside the kidney. Physiol Rev 2016; 96(2) 1327–1384.*
10. *Mazeh H, Froyshteter AB, Wang TS. Is previous same quadrant surgery a contraindication to laparoscopic adrenalectomy? Surgery 2012; 152: 7–11.*
11. *Taskin HE, Siperstein A, Mercan S. Laparoscopic posterior retroperitoneal adrenalectomy. J Surg Oncol 2012; 106(5): 619–21.*
12. *Lairmore TC, Folek J, Govednik CM. Improving minimally invasive adrenalectomy: selection of optimal approach and comparison of outcomes. World Jour Surg. 2016; 40: 1625–1631.*
13. *Chai YJ, Kwon H, Yu HW, et al. Systematic review of surgical approaches for adrenal tumors: lateral transperitoneal versus posterior retroperitoneal and laparoscopic versus robotic adrenalectomy. Int Jour Endocrinol. 2014; 2014: 2056-2066.*
14. *Marek-Safiejko M, Safiejko K, Lukaszewicz J, et al. A Comparison of two approaches to laparoscopic adrenalectomy: lateral transperitoneal versus posterior retroperitoneal approach. Adv Clin Exp Med. 2016;25: 829–835.*
15. *Lombardi CP, Raffaelli M, De Crea C, et al. Endoscopic adrenalectomy: Is there an optimal operative approach? Results of a single-center case-control study. Surgery. 2008;144:1008–1014. discussion 1014–1005.*
16. *Berber E, Tellioglu G, Harvey A, et al. Comparison of laparoscopic transabdominal lateral versus posterior retroperitoneal adrenalectomy. Surgery. 2009;146:621–625. discussion 625–626.*
17. *Lee CR, Walz MK, Park S, et al. A comparative study of the transperitoneal and posterior retroperitoneal approaches for laparoscopic adrenalectomy for adrenal tumors. Ann Surg Oncol. 2012; 19:2629–2634.*
18. *Economopoulos, K. P., Mylonas, K. S., Stamou, A. A., Theocharidis, V., Sergentanis, T. N., Psaltopoulou, T., & Richards, M. L. Laparoscopic versus robotic adrenalectomy: A comprehensive meta-analysis. Inter Jour of Surg 2017; 38, 95–104.*
19. *Bickenbach K, Strong, V. Laparoscopic transabdominal lateral adrenalectomy. Jour of Surg Onco. 2012; 106(5): 611–618.*
20. *National Comprehensive Cancer Network. (2015) NCCN clinical practice guidelines in oncology: neuroendocrine tumors. Version 1.2012 Available at: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.*
21. *Kaye DR, Storey BB, Pacak K et al. Partial adrenalectomy: underused first line therapy for small adrenal tumors. J Urol 2010; 184:18-204*
22. *Madala A, Daugherty M, Bratslavsky G. Partial adrenalectomy—why should it be considered? Urology Practice 2015; (2)1–8*