



Surgical treatment of adrenal tumours

Leczenie chirurgiczne guzów nadnerczy

Maciej Otto

Department of General, Vascular and Transplant Surgery, Medical University of Warsaw

Streszczenie

Wstęp: Operacje nadnerczy stały się obecnie najszybciej rozwijającą się dziedziną chirurgii endokrynologicznej. Wpływ na to, poza rozwojem technik chirurgicznych i wprowadzeniem metody laparoskopowej jako rutynowego leczenia operacyjnego zmian w nadnerczach, miały też inne czynniki. Należą do nich: rozwój diagnostyki endokrynologicznej i obrazowej oraz poznanie etiologii i zrozumienie wzajemnych uwarunkowań hormonalnych zmian w obrębie nadnerczy.

Materiał i metody: Na podstawie doświadczenia Kliniki Chirurgii Ogólnej, Naczyniowej i Transplantacyjnej WUM, w której w latach 1997–2009 wykonano 711 adrenalektomii (529 metodą laparoskopową, 182 metodą klasyczną) przedstawiono aktualne metody operacji nadnerczy, kwalifikacji oraz wskazań do leczenia operacyjnego.

Wyniki. Laparoskopowa adrenalektomia, potwierdzając swoje bezpieczeństwo i korzyści, zyskała aprobatę środowiska Medycznego, stając się podstawowym sposobem leczenia operacyjnego.

Wnioski.

1. Adrenalektomia wideoskopowa/laparoskopowa stała się operacją referencyjną w leczeniu zmian nadnerczowych.
2. Ścisła wielodyscyplinarna współpraca lekarzy biorących udział w leczeniu chorych ze zmianami nadnerczowymi spowodowała, że operacje nadnerczy stały się obecnie najszybciej rozwijającą się dziedziną chirurgii endokrynologicznej.

(*Endokrynol Pol* 2010; 61 (6): 716–722)

Słowa kluczowe: guzy nadnerczy, operacje nadnercza, adrenalektomia laparoskopowa

Abstract

Introduction: Nowadays operations of adrenal glands became the fastest-expanding field of the endocrine surgery. Besides the development of surgical techniques and introduction of laparoscopic method as a routine operating treatment of adrenal lesions, also other factors like a development of the endocrinological and imaging diagnosis together with the knowledge of etiology and understanding of hormonal interactions of the adrenal glands have contributed to it.

Material and methods: Based on experience of the Department of General, Vascular and Transplant surgery WUM where between 1997–2009 711 adrenalectomies were carried out (529 laparoscopic and 182 classical) current methods of adrenal operation, qualifications and indications were presented.

Results: Laparoscopic adrenalectomy confirming its safety and benefits has gained the approval of the medical fraternity and became the main method of surgical treatment.

Conclusions:

1. Videoscopic/laparoscopic adrenalectomy became the recommended operation in the treatment of adrenal lesions.
2. Close multidisciplinary cooperation of doctors participating in the treatment of patients with adrenal pathology has made the adrenal gland surgery the most rapidly developing field of the endocrine surgery.

(*Pol J Endocrinol* 2010; 61 (6): 716–722)

Key words: adrenal tumors, operations of the adrenal gland, laparoscopic adrenalectomy

Introduction

Surgery is the principal element of management of adrenal tumours detected by imaging studies. In pheochromocytoma, surgery is the treatment of choice, the only method that gives the patient a chance of cure and a method that makes it possible to avoid dangerous cardiovascular complications [1–4]. There has been an increasing change in therapeutic approach due to

the recent dynamic progress in endocrine diagnostics, a better understanding of the pathophysiology of endocrine disorders, and progress in the imaging evaluation of adrenal glands. This is also markedly reflected in the tactics and assumptions of surgical treatment, particularly since the introduction of microinvasive laparoscopic surgery in routine practice [5].

The beginnings of adrenal surgery date back to the late 19th century, when J.K. Thornton performed the



Prof. Maciej Otto MD, PhD, Department of General, Vascular and Transplant Surgery, Medical University of Warsaw, Warszawa 02-097, Banacha St.1a, mobil: 601 923 381, e-mail: maciej.otto@wum.edu.pl

first documented resection of an adrenal tumour in 1889. In 1926, independently, Cesar Roux in Switzerland and Charles Mayo in the US performed surgery for pheochromocytoma [2].

In this initial period of surgery the effect of adrenal tumours on the body was unclear and no uniform terminology was used. The role of surgery was therefore limited to resection of a tumorous adrenal gland. It was not until a better understanding of the aetiology and endocrine interrelationships was gained that the tactics of surgical management and surgical techniques could be developed [6].

The recognition of the metabolic nature of adrenal disorders has been the factor determining the possibilities of surgical treatment. The discovery and clinical application of cortisone in 1950 should therefore be considered the beginning of modern endocrinology and modern endocrine surgery. This was a breakthrough in our understanding of the pathophysiology of adrenal disorders, which ten years later led to the formulation of a hypothesis whereby the systemic homeostasis is jointly regulated by the nervous system and the endocrine system (neurohormones) [5]. This, in turn, made it possible to change the tactics of surgical management and broadened the scope of endocrine surgical procedures, especially adrenal surgery. The scope of adrenal resection became increasingly dependent on the intraoperative assessment, which necessitated visualisation of both glands.

The second half of the 20th century was a period of dynamic development for endocrine surgery, allowing surgeons to resect the gland to the extent necessary to restore hormonal balance, and to intervene before secondary systemic changes (preclinical endocrine syndromes, incidentaloma, ACTH-dependent hypercortisolaemia) could develop [5, 7].

The development of surgical methods is the result of attempts to use the least traumatogenic techniques and to perform the so-called targeted operations involving only the gland or the tumour responsible for a given pathology. This was possible thanks to advances in anatomy, physiology, and pathophysiology, progress in imaging techniques (ultrasound, scintigraphy, computed tomography, magnetic resonance imaging, positron emission tomography), and methods of restoring endocrine balance in the preoperative period. All these factors have contributed to the fact that adrenal surgery has now become the fastest growing area of endocrine surgery [8–11].

Currently the surgeon's intervention is not limited to a simple removal of the tumour but includes a well-informed resection taking into consideration the known endocrine implications. This state of affairs may be summarised by paraphrasing the Polish writer Bolesław

Prus: "The difference between a good and a bad writer is as follows: a bad writer writes what he knows, while a good one knows what he writes".

Methods of adrenal surgery

It seems that as far as the history of surgical techniques is concerned, the current possibilities of treatment of adrenal lesions have been principally influenced by three events. Firstly, by the report of simultaneous uncovering and operation of both adrenals through approaches along the spine, as described by H.H. Young in 1936, secondly by the presentation of the benefits of the transperitoneal approach in 1955 by Aird, and, thirdly, almost a century after the first documented adrenalectomy, by laparoscopic adrenal resection, as performed by L. Snow in 1991 [2, 5]. These three events have had a fundamental effect on the tactics of surgical treatment. The surgeon can now not only select the approach to the adrenal gland but also the surgical technique: classical or laparoscopic. The latter, through widespread acceptance, has had a tempestuous growth leading to the development, within the method, of comparable approaches to those in classical surgery. The principles and aims of surgical treatment have remained the same. The surgical approach depends on the cause of the pathology, tumour size, performance status, and the surgeon's experience [12].

The classical approaches in adrenal surgery include: anterior transperitoneal approach, abdominothoracic approach, anterolateral thoracic approach with incision of the diaphragm, lateral extraperitoneal approach, and posterior approach through the 10th, 11th, and 12th ribs. The most commonly used approaches at present are the anterior transperitoneal approach and the lateral or posterior extraperitoneal approach. The anterior transperitoneal approach is recommended for bilateral or ectopic lesions and for repeat surgery for pheochromocytoma and invasive tumours. The problem with this approach is the considerable extent of the cutaneous incision affecting the patient's comfort during the postoperative period and wound healing as a result of its reduced resistance to infection. The posterior approach from the lumbar muscles (extraperitoneal approach) is better tolerated by patients. There is a lower rate of infection with this approach. The thoracoabdominal approach and the anterolateral thoracic approach with incision of the diaphragm are rarely utilised and are indicated only in large malignant adrenal tumours [12, 13].

Laparoscopy has become the reference method in surgical management of adrenal glands despite continuing to raise certain objections in the case of malignant tumours. Nevertheless, numerous studies confirm that

Table I. Videoscopic approaches in adrenal surgery**Tabela I. Rodzaje dostępów wideoskopowych w operacjach nadnerczy**

Videoscopic access to the adrenal	Authors
Transperitoneal anterior Laparoscopic	Bońjer, Linos, Takeda Fernandez-Cruz
Transperitoneal lateral Laparoscopic	Higashihara, Gagner, Marescaux, Brunt, Jacobs
Retroperitoneal lateral	Mercan, Bońjer, Heintz, Fernandez-Cruz
Retroperitoneal posterior	Duh, Baba, Smith

the method allows one to respect the principles of oncologic surgery and to remove invasive tumours. For this reason the different variations of microinvasive adrenal resection have become an integral part of endocrine surgery and are considered the fundamental method of treatment. The approaches used in video-assisted adrenal surgery are summarised in Table I [8].

Each of the four methods differs in terms of approach, which is associated with various technical aspects of the procedure, although all of them share the same benefits of microinvasive surgery, namely a lower injuriousness resulting from a lower tissue traumatization and a better intraoperative anatomical visualisation translating into a higher peri- and postoperative comfort perceived by the patient. This leads to shorter hospitalisation, a more rapid recovery and resumption of life and professional activities, and a lower severity of postoperative pain. Another important factor is the cosmetic effect in the form of a smaller postoperative scar [10].

The most common laparoscopic approach, used in about 85% of adrenalectomies, is the lateral transperitoneal approach. It enables the surgeon to perform, before tissue preparation, a thorough assessment of the adrenal gland, to locate the tumour and its surrounding tissues, and carry out intraperitoneal diagnostics [1, 5, 8, 11].

As in the classical method, laparoscopy enables, according to the indications, bilateral simultaneous adrenalectomy (pheochromocytoma) or two-stage (syndromes associated with hypercortisolaemia) to be performed. Thanks to the increasing amount modern, technically reliable equipment, eliminating the inconvenience of laparoscopy (lack of the sense of touch), it is feasible to use sparing resection of the adrenal to preserve the adrenocortical function.

As a result, it is possible to avoid the use of permanent substitution therapy in patients who have undergone bilateral adrenalectomy. The indications for laparoscopy are, first of all, hereditary multiple endocrine neoplasia syndromes in which pheochromocytoma is one of their components. The opportunity to use intra-

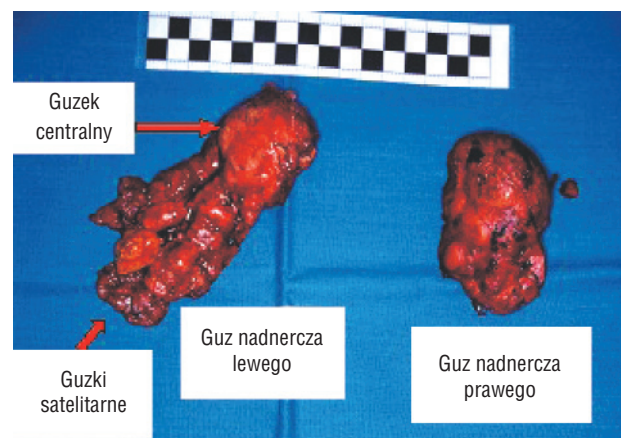


Figure 1. Bilateral pheochromocytoma: centre tumour with numerous satellite nodules

Rycina 1. Obustronne guzy chromochłonne: guz centralny z licznymi guzkami satelitarnymi

operative ultrasonography is very helpful in intraoperative decision making in this technique [4, 15, 16]. This allows the avoidance and resolution of problems associated with the sparing adrenalectomy, such as assessment of the line of resection, confirmation of the lesion resection, and the existence of neoplastic invasion.

Evaluation of the resection line defines radicality of tumour excision and the borderline of normal remaining adrenal cortex. The size of the operated tumour has an impact on this. Most favourable conditions for leaving the adrenal cortex well-supplied with blood have lesions with a diameter of no more than 2 cm. Relapses in classic sparing operations occur in 33% of patients with MEN II syndrome and in 15% with von Hippel Lindau syndrome [17–19].

Confirmation of lesion resection ensures the elimination of catecholamine excretion as well. In addition to the central tumour satellite lesions unrecognized in imaging studies may coexist (Fig. 1)

The last problem is the evaluation of neoplastic invasion. Assessment and diagnosis of malignant pheochro-

mocytoma is always a big clinical and pathomorphological problem. Pheochromocytoma is malignant in about 10% of cases (from 2.5–26%). Still the only sure confirmation of malignancy can give the presence of metastases to the lymph nodes and distant organs, which in physiological conditions do not contain chromaffin tissue. Infiltration of surrounding tissues and vessels does not directly indicate a malignant process. Factors that may suggest it are: young age, multiple lesions, extra-adrenal location (30–40%), tumour size more than 6 cm (although there is no threshold increasing the risk of malignancy), only dopamine-secreting tumours, and persistent postoperative hypertension. Another factor may also be the presence, of disease recurrence or relapse after the operation. After classical surgery, recurrence was found in 6–8% of patients.

According to many authors, only after 15 years of lack of recurrence following adrenalectomy due to pheochromocytoma can confirmation of the effectiveness of operations and exclusion malignancy be made. Sparing adrenalectomy results show no difference in the effectiveness of preservation of adrenal function, no matter if the adrenal vein is ligated or not [20, 21].

Qualification for adrenalectomy

Prior to the operation and the selection of surgical technique an accurate diagnosis should be determined. It is necessary to answer the question whether the observed lesion is or is not hormonally active; in the absence of activity, whether it is a benign or malignant; and if it is malignant, whether it is a primary or metastatic lesion. In every case it is desirable to determine the location of the tumour. In a situation of increased secretion of hormones, the preoperative preparation of patients is necessary:

- changes related to hypercortisolaemia — the absolute inhibition of excessive secretion of cortisone — steroidogenesis inhibitors;
- primary hyperaldosteronism — correction of the level of potassium in serum and normalization of blood pressure;
- pheochromocytoma — required normalization of blood pressure by the administration for 10–21 days of alpha receptor blocking agents and additional consideration of beta receptor blockade.

The preparation of pheochromocytoma is considered correct if blood pressure in the supine position above 160/90 mm Hg for 48 hours and orthostatic hypotension below 80/45 mm Hg is not found, and in addition, in ECG, if changes in the ST-T segment and T wave reversal for at least two weeks are not found, as well as premature beats - no more than one premature ventricular contraction every 5 minutes [22].

In incidentaloma type tumours cancer, metastases to the adrenal gland and increased secretion should be

ruled out. The surgical problem here is that the only reliable confirmation of malignant incidentaloma is given by histopathological examination performed after surgery. It is known that tumours removed in the early stages have a better prognosis than those removed at a more advanced stage. The prognosis after cancer diagnosis depends on the local tumour advancement at the time of diagnosis and the radicality of tumour resection during the first operation. Therefore, the operated tumour should be removed without damaging the capsule together with the entire gland and the surrounding adipose tissue [23]. Also, during the observation of the incidentaloma, not qualified for surgical treatment initially, any clinical change should dictate the type of surgery. Based on recent trends, this follow-up period should be four years. After this period, if no changes in phenotype of the tumour are noticed, observation can be discontinued [9].

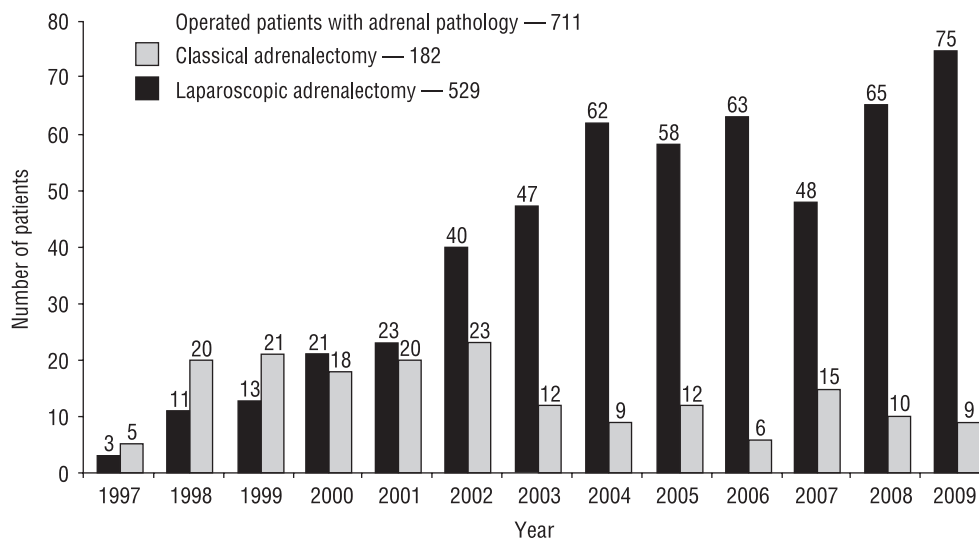
The risk of malignancy for hormonally inactive tumours (incidentaloma) is estimated at about 4–5%. If the diameter exceeds 4 cm, the risk increases in percentage and gradually increases with size. For tumours with a diameter above 4 cm, this risk is assessed at about 10%; for tumours larger than 6 cm it is 25–98%. Therefore, during qualification of lesions without hormonal activity, the basic criterion for surgical treatment remains the size of the tumour. The cutoff point is accepted at 4 cm [24, 25]. In some centres, since the introduction of laparoscopic adrenalectomy as a treatment method for adrenal lesions, tumours > 3 cm are eligible for surgery in young people with low-risk, and > 5 cm in elderly patients with concomitant diseases of other systems and organs [26].

Indications for adrenalectomy

Currently, in the presence of the two methods (classical and videoscopic-laparoscopic) of operation performed on adrenal glands, the range and the purpose of operation have not changed. Only the surgical access has been changed for the comfort of patients. Based upon experience confirmed by numerous clinical studies, classical surgery should remain the only treatment method for the so-called large tumours exceeding 10 cm, reoperation of the adrenal glands, and in the case of invasive carcinomas with signs of malignancy detected by imaging studies (features of local invasion, lymphadenopathy, distant metastases) and in the absence of an exact location — ectopic lesions [12, 13].

In other cases (hormonally active lesions, incidentaloma type tumours, metastatic tumours particularly metachronous), the videoscopic/laparoscopic method is the preferential method [23, 26]. This is also the case in our experience (Fig. 2).

The method of qualification of a patient with adrenal pathology is shown in Figures 3.



Rycina 2. Operated patients with adrenal pathology in the Department of General, Vascular and Transplant Surgery in the period 1997–2009

Figure 2. Operowani chorzy z patologią nadnerczy w Klinice Chirurgii Ogólnej, Naczyniowej i Transplantacyjnej WUM w okresie 1997–2009

Adrenalectomy preserving adrenocortical functions, which enables the avoidance of substitution treatment, is performed only in selected cases, especially in familial multiple endocrine neoplasia syndromes. Difficulties in the evaluation of neoplastic invasion of adrenal tumours remain the primary limitations of indications for such operations [23, 26]. The exact tumour size indicated for laparoscopic adrenalectomy/videoscopic is questionable [27].

Currently, during qualification for use of videoscopic techniques, the tumour size plays a decreasing role. It is recognized that even tumours with a diameter of up to 12 cm are not a contraindication for laparoscopic surgery [28]. Documented advantages of minimally invasive techniques are emphasized here, considering also that the association of indications with the size depends on the experience of the operating team and the limitations of the instrumentarium [28, 29].

Another factor influencing this opinion is the observation that imaging studies underestimate the actual size of the tumour — in computed tomography by 16 to 47%, and in magnetic resonance imaging by 20% [30–32].

Although laparoscopic lateral transperitoneal access is more frequently used and its larger versatility has been emphasised, the discussion is ongoing regarding the advantages and disadvantages of each of the methods of videoscopic access. However, the conclusions remain unchanged: endoscopic adrenalectomy is the method of choice, and both techniques (both trans- and retroperitoneal) are safe and give good results [33, 34].

The controversy also applies to the application of laparoscopic techniques in the surgery of malignant adrenal tumours. The opinion that classical adrenalectomy remains a technique reserved for large tumours with suspected malignancy is now challenged. Videoscopic adrenalectomy can be performed for malignant tumours, provided the principles of the oncological radicality are preserved. Its use in these cases should be determined by the experience and skill of the surgeon, and not by well-defined tumour size [35, 36].

Because of difficulties in the evaluation and diagnosis of malignancy, during videoscopic surgery the removal of the adrenal tumours from the peritoneal cavity through the wound should be carried out in a laparoscopic bag. In addition, it seems reasonable not to cut the tumour unnecessarily after surgery. Sending the intact tumour for pathomorphological testing sometimes facilitates difficult histological assessment of the lesion [1, 5].

Conclusions

1. Videoscopic/laparoscopic adrenalectomy has become the recommended operation in the treatment of adrenal lesions.
2. Close multidisciplinary cooperation of doctors participating in the treatment of patients with adrenal pathology has made adrenal gland surgery the most rapidly developing field in endocrine surgery.

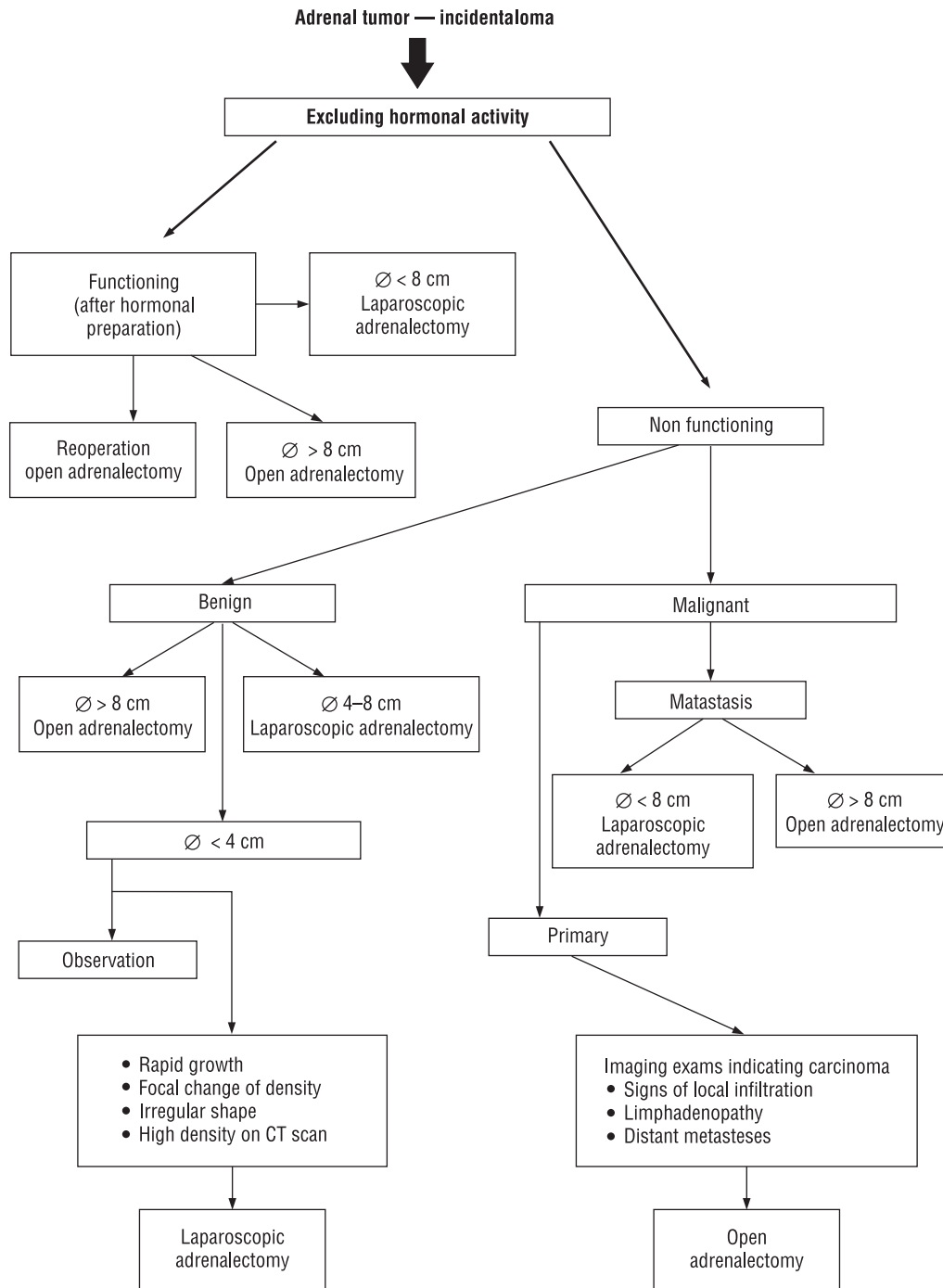


Figure 3. Algorithm qualification of adrenal lesions for adrenalectomy

Rycina 3. Algorytm kwalifikacji zmian nadnerczowych do adrenalectomii

References

- Otto M, Dzwonkowski J, Jędrasik M et al. Trudności kwalifikacyjne i operacyjne adrenalectomii laparoskopowej. *Pol Przegl Chir* 2010; 1: 64–78.
- Otto M. Operacyjne leczenie guzów nadnerczy. In: Szczepańska-Sadowska E, Sznajderman M, Januszewicz W, Januszewicz A (red.). *Nadciśnienie Tętnicze. Medycyna Praktyczna, Kraków 2007*: 849–859.
- Grupa Robocza Polskiego Towarzystwa Nadciśnienia Tętniczego. Wytyczne dotyczące diagnostyki i leczenia chorych z guzem chromochłonnym. *Nadciśnienie Tętnicze* 2006; 10: 1–19.
- Eisenhofer G. Pheochromocytoma: recent advances and speed bumps in the road to further progress. *J Hypertens* 2006; 24: 2341–2342.
- Otto M, Dzwonkowski J, Ciąćka T et al. Ponad 10-letnie doświadczenia w leczeniu zmian nadnerczowych metodą laparoskopową z dostępu bocznego przezotrzewnowego. *Pol Przegl Chir* 2008; 9: 881–894.
- Davis CJ. A history of endoscopic. *Surg Laparoscopy Endosc* 1992; 2: 16–19.
- Toniato A, Merante-Boschin I, Opocher G et al. Surgical versus conservative management for subclinical Cushing syndrome in adrenal incidentalomas. *Ann Surg* 2009; 3: 388–391.
- Smith CD, Weber CJ, Amwerson JR. Laparoscopic adrenalectomy: new gold standard. *World J Surg* 1999; 23: 389–396.
- Brunt LM, Moley JF. Adrenal incidentaloma. *World J Surg* 2001; 25: 905–913.
- Assalia A, Gagner M. Laparoscopic adrenalectomy. *Br J Surg* 2004; 91: 1259–1274.

11. Ogilvie JB, Duh QY. New approaches to the minimally invasive treatment of adrenal lesions. *Cancer J* 2005; 11: 64–72.
12. Miccolli P, Rafaelli M, Berti P. et al.: Adrenal surgery before and after the introduction of laparoscopic adrenalectomy. *Br J Surg* 2002; 89:779–782.
13. Staren ED, Prinz RA. Adrenalectomy in the era of laparoscopy. *Surgery* 1996; 120: 706–711.
14. Kaouk JH, Matin S, Bravo EL. Laparoscopic bilateral partial adrenalectomy for pheochromocytoma. *Urology* 2002; 60: 1100–1103.
15. Jeschke K, Janetschek G, Peschel R. Laparoscopic partial adrenalectomy in patients with aldosterone-producing adenomas: indications, technique and results. *Urology* 2003; 61: 69–72.
16. Neumann HP, Reincke M, Bender BU. Preserved adrenocortical function after laparoscopic bilateral adrenal sparing surgery for heredity pheochromocytoma. *J Clin Endocrinol Metab* 1999; 84: 2608–2610.
17. Neumann HP, Berger DP, Sigmund G et al. Pheochromocytomas, multiple endocrine neoplasia type 2 and von Hippel-Lindau disease. *N Engl J Med* 1993; 329: 1531–1538.
18. Pacak K, Ilias I, Adams KT et al. Biochemical diagnosis, localization and management of pheochromocytoma: focus on multiple endocrine neoplasia type 2 in relation to other hereditary syndrome and sporadic forms of the tumour. *J Int Med* 2005; 257: 60–68.
19. Walz MK. Extent of adrenalectomy for adrenal neoplasm: sparing (subtotal) versus total adrenalectomy. *Surg Clin N Am* 2004; 84: 743–753.
20. Diner EK, Franks ME, Behari A et al. Partial adrenalectomy: The National Cancer Institute experience. *Urology* 2005; 66: 19–23.
21. Walther MM, Herring J, Choyke P et al. Laparoscopic partial adrenalectomy in patients with hereditary forms of pheochromocytoma. *J Urolog* 2000; 164: 14–17.
22. Bravo EL. Pheochromocytoma: new concepts and future trends. *Kidney Int* 1991; 40: 544–551.
23. Kebebew E, Siperstein AE, Clark OH et al. Results of laparoscopic adrenalectomy for suspected and unsuspected malignant adrenal neoplasms. *Arch Surg* 2002; 137: 948–953.
24. Kasperlik-Zaluska AA, Otto M, Cichocki A et al. Incidentally discovered adrenal tumors: a lesson from observation of 1444 patients. *Horm Metab Res* 2008; 40: 338–341.
25. Kasperlik-Zaluska AA, Otto M, Cichocki A et al. 1,161 patients with adrenal incidentalomas: indications for surgery. *Langenbecks Arch Surg* 2008; 2: 121–126.
26. Sturgeon C, Kebebew E. Laparoscopic adrenalectomy for malignancy. *Surg Clin N Am* 2004; 84: 755–774.
27. Tsuru N, Suzuki K, Ushiyama T et al. Laparoscopic adrenalectomy for large adrenal tumors. *J Endourol* 2005; 19: 537–540.
28. Gumbs AA, Gagner M. Laparoscopic adrenalectomy. *Best Pract Res Clin Endocrinol Metab* 2006; 20: 483–499.
29. Parnaby CN, Chong PS, Chisholm L et al. The role of laparoscopic adrenalectomy for adrenal tumors of 6 cm or greater. *Surg Endosc* 2008; 22: 617–621.
30. Caoili EM, Korobkin V, Francis R. Adrenal masses: characterization with combined unenhanced and delayed enhanced CT. *Radiology* 2002; 222: 629–633.
31. Linos DA, Stylopoulos N. How accurate is computed tomography in predicting the real size of adrenal tumors? A retrospective study. *Arch Surg* 1977; 132: 740–743.
32. Lau H, Lo CY, Lam KY. Surgical implications of underestimation of adrenal tumour size by computed tomography. *Br J Surg* 1999; 96: 385–387.
33. Tai CK, Li SK, Hou SM et al. Laparoscopic adrenalectomy: Comparison of lateral transperitoneal and lateral retroperitoneal approaches. *Surg Laparosc Endosc Percutan Tech* 2006; 16: 141–145.
34. Rubinstein M, Gill IS, Aron M. Prospective randomized comparison of transperitoneal versus retroperitoneal laparoscopic adrenalectomy. *J Urol* 2005; 174: 442–445.
35. Lombardi CP, Raffaelli M, De Crea C et al. Role of laparoscopy in the management of adrenal malignancies. *J Surg Oncol* 2006; 1: 128–131.
36. Barnett CC, Varma DG, El-Naggar AK. Limitation of size as a criterion in the evaluation of adrenal tumors. *Surgery* 2000; 128: 973–982.