

Adrenalectomy for benign and malignant adrenal tumors. Experience from Misurata Cancer Center

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SUMMARY: Adrenalectomy for benign and malignant adrenal tumors. Experience from Misurata Cancer Center.

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Background. Laparoscopic adrenalectomy is the standard management of benign adrenal tumors. Open adrenalectomy is still the gold standard surgical treatment for adrenocortical carcinoma and malignant pheochromocytoma, while the role of minimal invasive surgery is still controversial. Laparoscopic adrenalectomy is associated with low morbidity rate, short hospital stay and rapid recovery to work. The aim of the study is identifying the advantages of laparoscopic adrenalectomy in comparison to open adrenalectomy.

Methods. We present a retrospective study of 21 adrenal tumors that underwent surgical resection at Misurata Cancer Center from April 2013 up to April 2018. We compared: age, sex, marital status,

past medical history, function and size of the tumor, type of surgery, duration of surgery, estimated blood loss, preparation of patient for surgery, post-operative complications, post-operative discharge day and mortality.

Results. There were 21 adrenal tumors, 61.9% were females and 38.1% were males, median age 41 years. 61.9% were hypertensive patients, 71.4% functional tumors and 28.6% nonfunctional tumors. 71.4% benign tumors and 28.6% malignant. Laparoscopic adrenalectomy was done in 15 cases (71.4%), open adrenalectomy in 6 cases (28.6%), and 4 cases (19%) were converted to open surgery. Morbidity was 19%, and 30 days mortality rate was 4.7%.

Conclusion. Surgical treatment of adrenal tumors consists of laparoscopic and open adrenalectomy. The type of surgery depends on the size of the tumor and suspicious of malignancy in imaging study. Laparoscopic adrenalectomy is safe and effective for benign tumors with decreased operative time, less post-operative pain, and decreased hospital stay.

KEY WORDS: Laparoscopic adrenalectomy - Pheochromocytoma - Functional adenoma.

Introduction

Laparoscopic adrenalectomy is the gold standard treatment of both functioning and nonfunctioning benign adrenal tumors of less than 6 cm in size (16, 21). Open adrenalectomy is still the treatment of choice for malignant neoplasm of adrenal gland (17, 21). Laparoscopic adrenalectomy has many advantages, including decreased the length of hospital stay, reduced postoperative pain, and early return to work (13, 14). Laparoscopic adrenalectomies can be done by transabdominal or retroperitoneal ap-

proaches. The choice depends on the size of the tumor and expertise of the surgeon (11). Open adrenalectomy can be done by anterior transabdominal approach via long midline incision or long subcostal incision, and posterior retroperitoneal approach via incision at bed of 12th rib with the patient lying prone. Open surgery is associated with more pain, ileus, atelectasis, longer period of recovery, and increase risks of poor wound healing, especially for patient with Cushing syndrome (16).

Functioning adenoma is indication for adrenalectomy. Pheochromocytoma is a functional tumor of adrenal medulla secreting catecholamines causing symptoms of hypertension in form of headache, palpitation, and diaphoresis. Conn's adenoma is a tumor of adrenal cortex where Zona Glomerulosa secreting excess of aldosterone causes symptoms of hypertension, fatigability and muscle weakness due to

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hypokalemia. Cushing adenoma is tumor of adrenal cortex where Zona Fasciculata secreting excess of Cortisol causing symptoms of Cushing syndrome, truncal obesity, hirsutism, moon face, acne, striae, buffalo hump, hypertension, and diabetes (1).

Laboratory tests used to identify the adrenal function including tests for serum metanephrine and noremetanephrine are of 99% sensitive and 89% specific, and 24hr urine collection of catecholamine and their metabolites are 88% sensitive and 95% specific for pheochromocytoma (4, 18). Conn's adenoma is diagnosed by high serum aldosterone level, high serum aldosterone/serum renin ratio, and low serum potassium level (1, 8). Cushing adenoma is diagnosed by high level of 24 hour urinary free cortisol, high serum cortisol and low serum ACTH (9, 12).

Radiological imaging is useful to reach the diagnosis of adrenal lesion and differs between benign and malignant feature (9). Contrast enhanced CT scan is useful imaging modality. The criteria of benign lesions are size <4 cm, homogenous, well defined borders, rapid washout of contrast, low vascularity, and high level of intracellular lipids. The criteria of malignant lesions are size >6 cm, heterogeneous, ill-defined borders, necrosis, calcification and hemorrhage within the mass, high vascularity and low level of intracellular lipids (2, 12).

Aims and objectives of the study

Advantages of laparoscopic adrenalectomy in comparison to open adrenalectomy as regards the operative time, less post-operative pain and hospital stay.

Patients and methods

From April 2013 to April 2018, we studied a series of adrenalectomies performed at the Misurata Cancer Center, Department of Surgical Oncology, Misurata, Libya. This study involved 21 patients with various adrenal tumors. The two types of surgery were used, transperitoneal laparoscopic and open adrenalectomies. Diagnosis was obtained on the basis of clinical examination, laboratory values and imaging techniques (Computed Tomography and Magnetic Resonance Imaging).

Patients evaluation included preoperative, intraoperative and post-operative data.

All patients underwent routine laboratory tests (complete blood count, urea, creatinine, sodium, potassium, blood sugar), and hormonal tests for adrenal function (serum metanephrine, serum noremetanephrine, serum aldosterone, serum renin, aldosterone renin ratio, serum and urine cortisol), chest X-ray, ECG, and cardiological evaluation. Patients diagnosed with Pheochromocytoma underwent an alpha blocker-Prazosin 7 to 10 days until blood pressure was controlled and patients developed postural hypotension, then tachycardia treated with beta blocker-Propranolol until heart rate became less than 100bpm. Also plasma volume expanded using crystalloid solutions. Patient diagnosed with Conn's adenoma with low serum potassium level, underwent potassium sparing diuretics Spironolactone and potassium chloride until serum potassium level returned to normal.

Intraoperative management: all patients received general anesthesia, antithrombotic prophylaxis (Fraxiparine 2500 I.U. s.c), and antibiotic prophylaxis (Ceftriaxone i.v.). In patients with pheochromocytoma arterial line is used for invasive monitoring of blood pressure intraoperatively. In laparoscopic adrenalectomy the patients were placed in lateral position with angle of 60 degree, using 4 trocars. Pneumoperitoneum initiated with Veress needle technique and maintained at 13-14 mmHg by insufflation of Carbon dioxide. In laparoscopic approach we used a combination of monopolar cautery and ligasure for dissection.

For right laparoscopic adrenalectomy monitor were placed at right shoulder of the patients while surgeon and assistant stand on the left side of the patient. The site of the trocars was the first one at anterior axillary line 2 finger breadth below the costal margin, this was the site of the camera where we used 10 mm 30 degree scope; second one at mid axillary line just below costal margin 5 mm trocar for left hand instrument of the surgeon; third one at midclavicular line just below the costal margin 5 mm trocar for the instrument of the right hand of the surgeon; fourth one at epigastric area 5 mm trocar for liver retractor. We started dissection by elevating liver by laparoscopic retractor then releasing the liver from upper pole of the gland by using of monopolar cautery, then we started dissection at

medial side of the inferior vena cava until we identified the adrenal vein where it is usually sited at upper medial part of the gland posterolateral to inferior vena cava. We use laparoscopic clips for ligation of the vein, two clips medially and one laterally then we cut in between by scissors. Then dissection by "ligasure" started up to right renal vein inferiorly and ligation of superior, middle and inferior adrenal arteries by ligasure. Medial to lateral dissection until the gland removed from its bed, specimen extracted through retrieval bag through mini laparotomy incision, one tube drain inserted at sub-hepatic area.

In left laparoscopic adrenalectomy the monitor were placed at left side of the patient while surgeon and assistant were at right side of the patient. The sites of the trocars were the first one at anterior axillary line hand breadth below costal margin for the camera 10 mm 30 degree scope, second one at mid clavicular line 2 finger below costal margin for left hand instrument of the surgeon 5 mm trocar, third one at mid axillary line just below costal margin 5 mm trocar for the instrument of the right hand of the surgeon. We start dissection by mobilization of splenic flexure, lateral attachments of the spleen are taken down, care must be taken to avoid capsular tear. Splenic mobilization continued until the greater curvature of the stomach and left crus of diaphragm became visible, taking care not to injury the pancreatic tail. Dissection continued up to left renal vein inferiorly. Identification of adrenal vein joining the inferior phrenic vein. Adrenal vein ligated with two clips medially and one laterally and cut in between with scissors, dissection of the gland with ligasure sealed the small superior, middle and inferior adrenal arteries. Dissection of the gland circumferentially until removed from its bed and extracted through retrieval bag through a mini laparotomy incision. Tube drain inserted at peri-splenic area.

Post-operative management: all patients received i.v. fluid in form of crystalloids, analgesia and vital sign monitoring. Patient with Cushing syndrome received i.v. hydrocortisone which started after removal of the cushing adenoma. Early mobilization in the same day of surgery and feeding started in first post-operative day for laparoscopic surgery, while mobilization is delayed until the first post-operative day in open surgery due to post-operative pain.

Results (Table 1, Figures 1-4)

There were 21 adrenal tumors, 13 were females (61.9%), and 8 were males (38.1%). The age of patients was classified equal and less than 40 years and other group more than 40 years, 11 were >40 years (52.3%), and 10 were <40 years (47.7%). Patients classified geographically as 8 (38.1%) were lived in Misurata city and 13 (61.9%) lived outside the city. Most common symptoms was headache seen in 7 patients (33.4%); all patients were hypertensive. Functional tumor seen in 15 cases (71.4%), non-functional tumors in 6 cases (28.6%). Malignant tumors seen in 6 cases (28.6%), benign tumors in 15 cases (71.4%).

Pheochromocytoma seen in 4 cases (19.05%); Conn's adenoma seen in 3 cases (14.2%); Cushing syndrome in 4 cases (19.05%); malignant pheochromocytoma in 4 cases (19.05%); incidentoloma in 4 cases (19.05%); adrenocortical carcinoma in 2 cases (9.6%). Serum potassium level were low in 3 cases (14.3%), normal in 18 cases (85.7%). Hypertension seen in 13 patients (61.9%), while in 8 patients blood pressure was normal (38.1%). Right adrenal tumor in 14 cases (66.6%), left adrenal tumor in 7 cases (33.4%). The size of the tumor was in 9 cases equal or less than 4 cm (42.9%), and in 12 cases were more than 4 cm (57.1%). MRI was done only in 5 cases (23.8%).

Laparoscopic adrenalectomy done in 14 cases (66.6%); open adrenalectomy in 7 cases (33.4%); 3 cases converted to open (14.3%). Operative time divided in two groups, one less than 2 hours 11 cases (52.4%), ten of them were laparoscopic (91%) and one of them was open (9%). The more than 2 hours group was 10 cases (47.6%), four of them were laparoscopic (40%), six of them were open (60%), $P=0.05$. Preoperative preparation for 10 cases (52.4%) and 11 cases with no need for preparation (47.6%). Early ambulation in same day of surgery were 11 cases all of them were laparoscopic, $P=0.0005$. CT scan and histopathological measurement were same in 2 cases (14.3%), while the sizes were more by one or half centimeter in histopathological measurement in 18 cases (85.7%). Patients discharged in postoperative day 3 or less were 11 cases (52.4%), all were laparoscopic cases (100%). Patients discharged in postoperative day >3 were 10 cases (47.6%), three of them were laparoscopic (30%), while seven of them

were open (70%), P=0.0002. Thirty days mortality was (4.7%).

Discussion

The first successfully LA was performed by Gagner in 1991. At present the transperitoneal approach is the most common surgery for adrenal tumors. The suspected primary malignant adrenal tumors should be considered for open resection, but still the best surgical approach is a matter of debate. The suspicious of malignancy was identified by preoperative imaging on CT scan with: local invasion of adjacent structures, distant metastasis, size >6cm, irregular borders, hemorrhage within the mass, low level of intracellular lipid, and high vascularity.

In our cases 21 adrenal tumors were female, the ratio was 2:1, but the incidence in the literature was same (1-4). The age of patients was >40 years (52.3%), and <40 years (47.7%). The average age by American Cancer Society is 46 years. The most common symptom was headache (33.4%), the most commonly adrenal tumors incidentally discovered with other symptoms (1-6). The most common tumors in our research were functional tumors

TABLE 1 - DEMOGRAPHICS.

Demographics	Number	%
Female	13	61.9%
Male	8	38.1%
>40 years	11	52.3%
<40 years	10	47.7%
Right	14	66.6%
Left	7	7%
<4 cm	9	42.9%
>4 cm	12	57.1%
Hypertensive	13	61.9%
Non hypertensive	8	38.1%

(71.4%), nonfunctional tumors (28.6%). In American Cancer Society and literature (1-12) the non-functional tumors were most common (60% of adrenal tumors). Malignant tumors seen 28.6%, benign tumors 71.4%, same as in American Cancer Society and literature (12-15) where benign tumors >90% of cases. Pheochromocytoma seen in 19.05%,

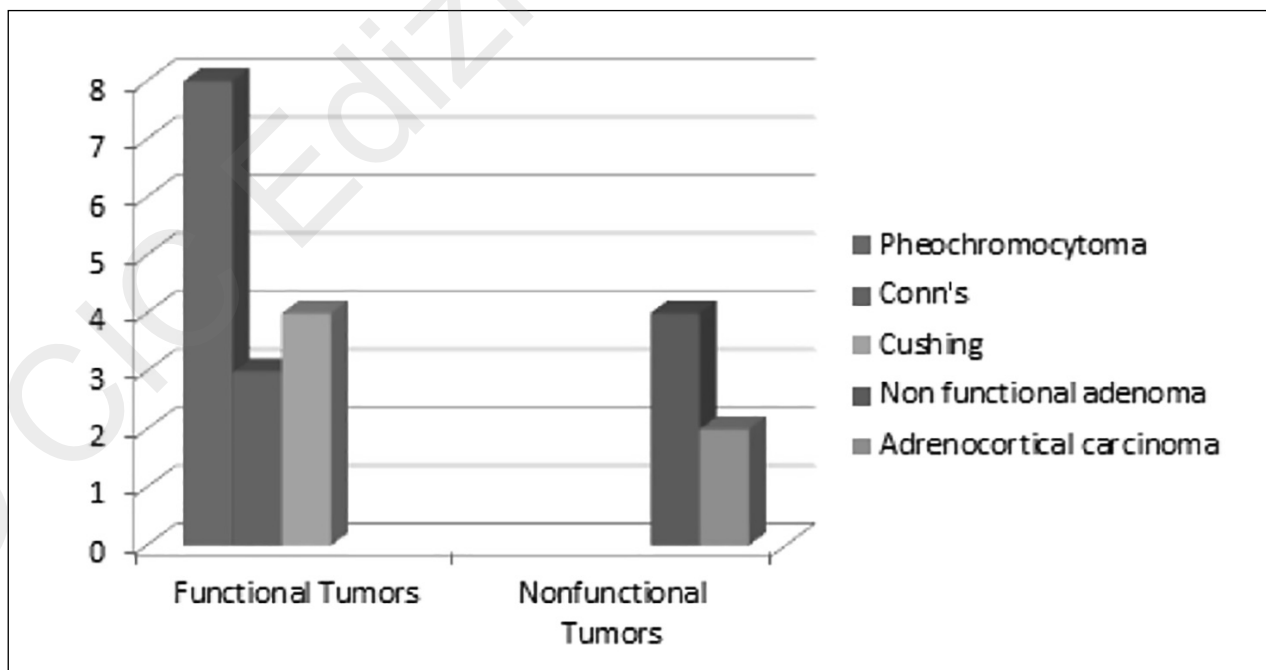


Figure 1 - Indication of surgery.

in literature pheochromocytoma were 10% (18). Conn's adenoma seen in 14.2%, in literature Aldosteronoma were 1% (8). Cushing syndrome seen in 19.05%, in America (1) the cortisol producing adenoma were 5%. Malignant pheochromocytoma seen in 19.05%, in literature (20) the malignant pheochromocytoma were 4%. Incidenteloma seen in 19.05%, in (11) the non functioning adenoma were 60%. Adrenocortical carcinoma seen in 9.6%, in literature (21) the adrenocortical carcinoma were 5%. Right adrenal tumor were in 66.6%, left adrenal tumor in 33.4%, so right adrenal tumor were more common in our research and same to the literature (16). The size of the tumor were equal or less than 4 cm (42.9%), all these cases were benign, more than 4 cm (57.1%), malignant tumors seen in 6 cases and all of them >9 cm. MRI were done for only 23.8%, other cases MRI not done due to unavailability. Laparoscopic adrenalectomy done in 66.6%, open adrenalectomy in 33.4%, three cases converted to open (14.3%), the first case due to bleeding liver injury which cannot be controlled laparoscopically, the second case due to bleeding from splenic tear, and the third case due to multiple intraabdominal adhesions due to previous open right hemicolectomy. Operative time divided in two groups, less than 2hours group were 52.4%, 91% laparoscopic and 9% open, more than 2 hours group were 47.6%, four of them were laparoscopic (40%), six were open (60%), so we found that the laparoscopic approach

was associated with less operative time. Post-operative blood sugar level seen low in 2 cases (9.5%), normal in 15 cases (71.5%) and high in 4 cases (19%). Patient discharged in post-operative day 3 or less were 52.4%, all were laparoscopic cases (100%). Patients discharged in post-operative day >3 were 47.6%, 3 of them were laparoscopic (30%), while 7 of them were open (70%), so in our research we found that the laparoscopic adrenalectomy associated with less hospital stay as in the literature (1-7). In comparison of the size of adrenal tumors between CT scan and histopathological measurement were same in 2 cases (14.3%), while the sizes were more by one or half centimeter in histopathological measurement in 18 cases (85.7%). Our complications rate were 19.1% while in literature (2-5) were 13-27%. Thirty days mortality was 4.7% in our research, while 2.2% in literature (17).

Conclusion

Surgical treatment of adrenal tumors consists of laparoscopic and open adrenalectomy. The type of surgery depends on the size of the tumor and suspicious of malignancy in imaging study, laparoscopic adrenalectomy is safe and effective for benign tumors with decreased operative time, less postoperative pain, and decreased hospital stay.

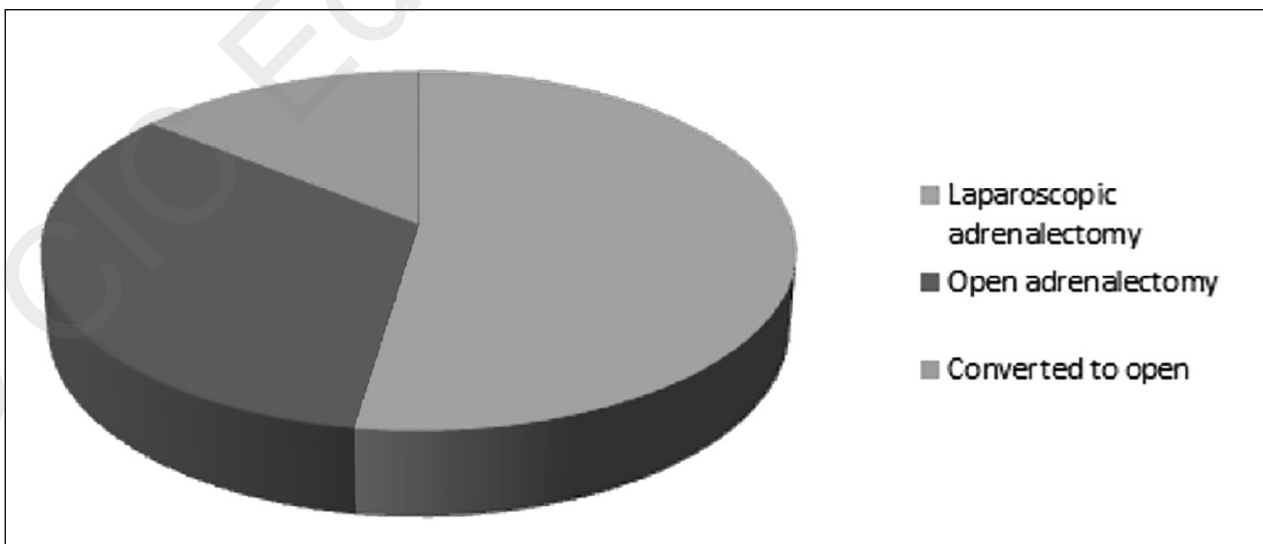


Figure 2 - Type of surgery.

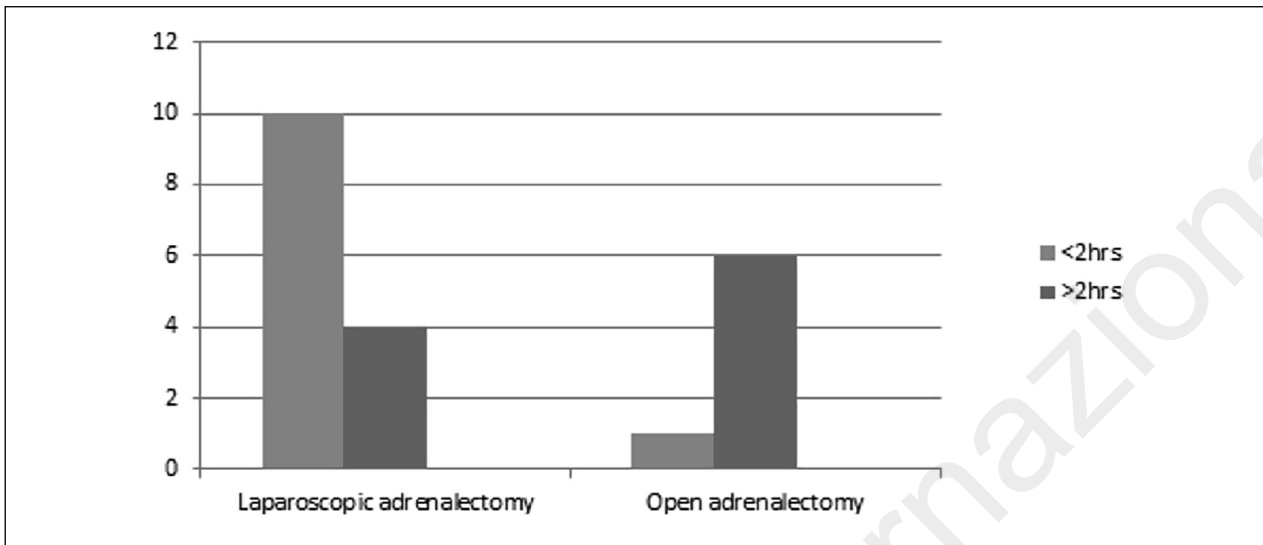


Figure 3 - Operative time.

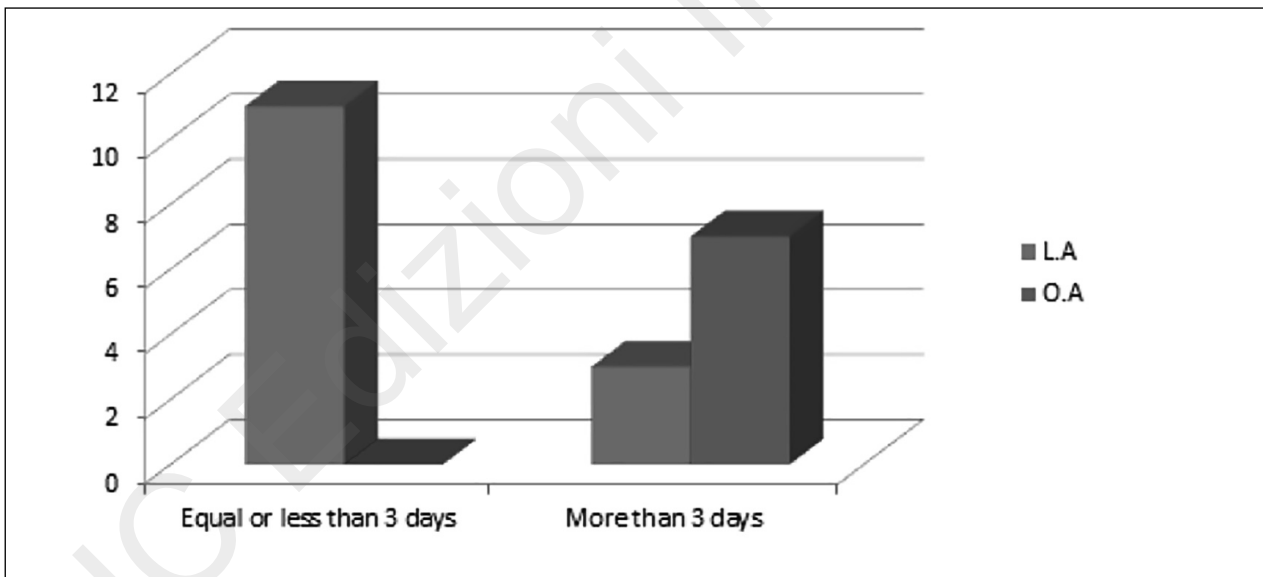


Figure 4 - Postoperative discharge days.

References

1. Townsend CM, Beauchamp RD, Evers BM, Mattox K. Sabiston textbook of surgery, 19th edition. 2012:963-993.
2. White ML, Gauger PG, Doherty GM, et al. The role of radiologic studies in the evaluation and management of primary hyperaldosteronism. Surgery. 2008;144:926-933.
3. Welbourn RB. Early surgical history of pheochromocytoma. Br J Surg. 1987;74:594-596.
4. Kudva YC, Sawka AM, Young WF Jr. Clinical review 164: The laboratory diagnosis of adrenal pheochromocytoma: The Mayo Clinic experience. J Clin Endocrinol Metab. 2003;88:4533-4539.
5. Imani F, Agopian VG, Auerbach MS, et al. 18F-FDOPA PET and PET/CT accurately localize pheochromocytomas. J Nucl Med. 2009;50:513-519.
6. Lenders JW, Pacak K, Walther MM, et al. Biochemical diagnosis of pheochromocytoma: Which test is the best? JAMA.

- 2002;287:1427-1434.
7. Shen WT, Lee J, Kebebew E, et al. Selective use of steroid replacement after adrenalectomy: Lessons from 331 consecutive cases. *Arch Surg.* 2006;141:771-774.
 8. Sukor N, Kogovsek C, Gordon RD, et al. Improved quality of life, blood pressure, and biochemical status following laparoscopic adrenalectomy for unilateral primary aldosteronism. *J Clin Endocrinol Metab.* 2010;95:1360-1364.
 9. de Virgilio C, Grigorian A, Frank PN. Surgery: A Case Based Clinical Review. 2015;8:77-87.
 10. Young WF. Clinical practice. The incidentally discovered adrenal mass. *N Engl J Med.* 2007;356(6):601-10.
 11. Terzolo M, Bavio S, Pia A, Reimondo G, Angeli A. Management of adrenal incidentaloma. *Best Pract Res Clin Endocrinol Metab.* 2009;23(2):233-43.
 12. Gagner M, Lacroix A, Bolte E. Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. *N Engl J Med.* 1992;327:1033.
 13. Jacobs JK, Goldstein RE, Geer RJ. Laparoscopic adrenalectomy. A new standard of care. *Ann Surg.* 1997;225:495-501; discussion 501-502.
 14. Smith CD, Weber CJ, Amerson JR. Laparoscopic adrenalectomy: new gold standard. *World J Surg.* 1999;23:389-396.
 15. Marescaux J, Mutter D, Vix M, et al. Endoscopic surgery: ideal for endocrine surgery? *World J Surg.* 1999;23:825-83412.
 16. Hallfeldt KJ, Mussack T, Trupka A, Hohenbleicher F, Schmidbauer S. Laparoscopic lateral adrenalectomy versus open posterior adrenalectomy for the treatment of benign adrenal tumors K. *Surg Endosc.* 2003;17:264-267.
 17. Barreca M, Presenti L, Renzi C, Cavallaro G, Borrelli A, Stipa F, Valeri A. Expectations and Outcomes When Moving from Open to Laparoscopic Adrenalectomy: Multivariate Analysis. *World J Surg.* 2003;27:223-228.
 18. Walz MK, Alesina PF, Wenger FA, et al. Laparoscopic and retroperitoneoscopic treatment of pheochromocytomas and retroperitoneal paragangliomas: results of 161 tumors in 126 patients. *World J Surg.* 2006;30:899-908.
 19. Kazaryan AM, Kuznetsov NS, Shulutko AM, Beltsevich DG, Edwin B. Evaluation of endoscopic and traditional open approaches to pheochromocytoma. *Surg Endosc.* 2004;18:937-41.
 20. Toniato A, Boschin IM, Opocher G, Guolo A, Pelizzo M, Mantero F. Is the laparoscopic adrenalectomy for pheochromocytoma the best treatment? *Surgery.* 2007;141:723-7.
 21. Lal G, Duh QY. Laparoscopic adrenalectomy - indications and technique. *Surg Oncol.* 2003;12:105-23.
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