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J.-F. Henry
T. Defechereux
L. Gramatica
M. Raffaelli

Should laparoscopic approach be proposed for large and/or potentially malignant adrenal tumors?

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J.-F. Henry (✉) · T. Defechereux
L. Gramatica · M. Raffaelli
Department of Endocrine Surgery,
University Hospital La Timone,
Bd J. Moulin,
F-13385 Marseilles Cedex 05, France
Tel.: +33-4-91385854
Fax: +33-4-91489637

Abstract *Introduction:* Laparoscopic adrenalectomy (LA) is safe and effective for small, benign, functioning tumors. Whether it should be performed for other adrenal tumors is questionable. The aim of this study was to evaluate and compare the complications and results of 150 consecutive LAs performed either for small benign tumors or for large and/or potentially malignant tumors. *Methods:* Between June 1994 and August 1998, we performed 150 LAs in 142 patients. We used a transperitoneal flank approach in the lateral decubitus position. Initially, our indications for LA were limited to small (<4 cm) benign tumors (group I, *n*=102): 56 aldosteronomas, 33 Cushing's syndrome, 11 pheochromocytomas and 2 nonfunctional tumors. Progressively, based on increasing experience, LA was also proposed for tumors larger than 4 cm or potentially malignant (group II, *n*=48): 5 Cushing's syndrome, 1 androgen-producing tumor, 14 pheochromocytomas and 28 nonfunctional tumors. Preoperative demonstration of invasive extra-adrenal carcinoma remained an absolute contraindication for LA. *Results:* Mean tumor size was 21.1 mm in group I and 51.6 mm in group II. All tumors in group I were benign. Six of the 48 tumors in group II were malignant (12.5%). The rate of complication was, respectively, 7.8% and 8.3% in groups I and II. The rate of conversion was, respectively, 4.9% and 6.2% in groups I and II. Mean operative time was 131 min in group I and 129 min in group II. The endocrinopathy was cured in all patients. To date, no recurrences have been observed. *Conclusions:* LA can be proposed for large (<12 cm) or potentially malignant adrenal tumors provided preoperative investigations have not demonstrated invasive carcinoma. An open procedure should be performed instead if local invasion is observed at the start of the operation.

Key words Laparoscopic adrenalectomy · Malignant · Adrenal tumor

Introduction

During the last 5 years, the advantages of a laparoscopic approach in adrenal surgery have been reported. Currently, one can consider that laparoscopic adrenalectomy (LA) is the procedure of choice for small, benign and functioning tumors. However, whether LA should be proposed for other adrenal tumors and particularly for large or potentially malignant tumors remains questionable. The aim of this study was to evaluate and compare the complications and results of 150 consecutive LAs performed either for small benign tumors or for large and/or potentially malignant tumors.

Table 1 Indications for open and laparoscopic adrenalectomies

Open adrenalectomies	48 (24.2%)
Large/malignant tumors	26
Multiple/extra adrenal pheochromocytomas	12
Previous surgery	10
Laparoscopic adrenalectomies	150 (75.8%)
Conn's syndrome	56
Cushing's syndrome	38
Androgen-producing tumor	1
Pheochromocytoma	25
Nonfunctional tumor	30
Total	198–100%

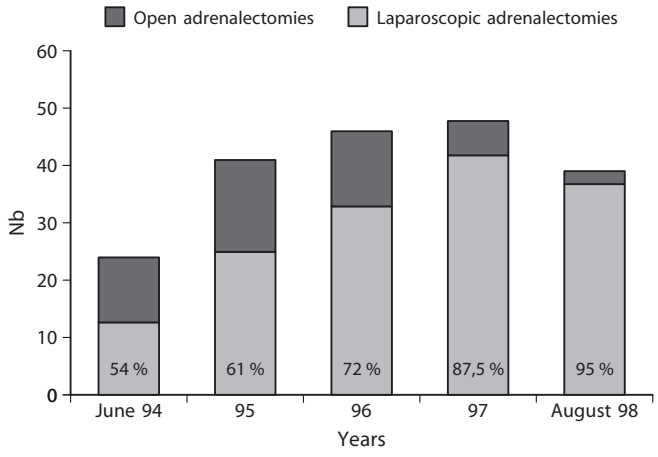

Fig. 1 Percentage of Laparoscopic adrenalectomies per years between 94 to 98

Material and methods

We started to use LA in June 1994. Between June 1994 and August 1998, we performed 198 adrenalectomies in our department. LA was performed by a transperitoneal flank approach in the lateral decubitus position as it was first described by Gagner [1, 2]. At the beginning of our study, our indications for LA were limited to small and functioning tumors [3]. Progressively, based on our increasing experience, LA was also proposed for tumors larger than 4 cm in diameter. Preoperative demonstration of invasive extra-adrenal carcinoma remained an absolute contraindication for LA. An open approach was used in 48 cases (24.2%; Table 1): large and/or malignant or suspected malignant tumors (26 cases), multiple and/or extra-adrenal pheochromocytomas (12 cases) and patients who had had previous surgery in the adrenal area (10 cases).

LA was proposed in 150 cases (75.8%; Table 1). LA was used in 54% of cases the first year, in 61% in 1995, 72% in 1996, 87.5% in 1997 and in 95% of cases during the first eight months of 1998 (Fig. 1). Among patients operated on by LA, we compared two groups: group I consisted of patients presenting tumors smaller than 4 cm in diameter and benign; group II consisted of patients with tumors larger than 4 cm in diameter or known malignancies (metastases) or potential malignancies. Malignancy was not only suspected when tumors were larger than 4 cm; biochemical function, appearance in computed tomography (CT) scan or magnetic resonance imaging (MRI) and history of extra-adrenal cancer were also taken into account. For most of the tumors in group II, pre-operative studies were not definitively diagnostic for malignancy or benignancy.

Table 2 Indications for laparoscopic adrenalectomy in group I (tumor <4 cm, benign) and in group II (tumor >4 cm, potentially malignant)

Endocrine disease	Group I	Group II	Total
Conn's syndrome	56	–	56
Cushing's syndrome	33	5	38
Androgen-producing tumor	–	1	1
Pheochromocytoma	11	14	25
Nonfunctional tumor	2	28	30
Total	102	48	150

In group I (102 cases), there were 56 patients with Conn's syndrome, 33 with Cushing's syndrome, 11 pheochromocytomas and 2 nonfunctional tumors. In group II (48 cases), there were 5 patients with Cushing's syndrome, 1 androgen-producing tumor, 14 pheochromocytomas and 28 nonfunctional tumors (Table 2). Mean tumor size was 21.1 mm in group I (7–39 mm) and 51.6 mm in group II (35–110 mm). Pre-operative preparation with nicardipine and intra-operative nicardipine infusion were used to help control the blood pressures of patients with pheochomocytoma. Nevertheless, fluctuations in blood pressure occurred in more than half of our 25 patients with pheochromocytoma.

Results

All tumors in group I were benign at final histology. However, 6 of the 48 tumors in group II were malignant (12.5%). Three of these six malignant tumors were completely removed laparoscopically; these included one metastasis, one leiomyosarcoma (40 mm) and one androgen-producing tumor (35 mm). In the last case, malignancy was demonstrated by vascular invasion of the proximal portion of the left adrenal vein of the specimen. Conversion to open surgery was required in the three other cases. In four cases, malignancy was suspected or confirmed at the start of the procedure; these included three metastases (two conversions) and one adreno-cortical carcinoma (a conversion). In these cases, suspicion of malignancy was based on the difficulties of dissection, dense adhesions, consistency of the tumor or unusual and numerous retroperitoneal feeding vessels.

At follow-ups of 4 years, 4 years and 1 year, patients with the leiomyosarcoma and the two adreno-cortical carcinomas, respectively, were disease free; tumor markers were negative and there was no evidence of local recurrence. The three patients in which LA was attempted to cure a solitary adrenal metastasis had known primary cancers (two in the lungs, one in the colon) that had been completely resected previously. The follow-up was of less than 1 year.

An open operation was performed instead in five patients in group I (4.9%) because of difficulties of dissec-

Table 3 Complications of laparoscopic adrenalectomies in group I (tumor <4 cm, benign) and in group II (tumor >4 cm, potentially malignant)

Complications	Group I (*n*=102)	Group II (*n*=48)
Peroperative bleeding	1	2
Peritoneal hematoma	2	1
Parietal hematoma	1	–
Tumor effraction	–	1
Spleen infarction	1	–
Pneumothorax	1	–
Deep venous thrombosis	2	–
Total	8 (7.8%)	4 (8.3%)

Table 4 Comparison of results of laparoscopic adrenalectomies in group I (tumor <4 cm, benign) and in group II (tumor >4 cm, potentially malignant)

Results	Group I	Group II
Mean tumor size	21.1 mm	51.6 mm
Mean operative time	131 min	129 min
Malignancy	0%	12.5%
Complications	7.8%	8.3%
Conversions	4.9%	6.2%

tion in four cases and pneumothorax in one. In group II, three patients (6.2%) required a laparotomy due to malignancy. Eight patients in group I (7.8%) had significant complications: one parietal hematoma, two peritoneal hematomas (requiring re-operation in one case), two deep venous thromboses, one pneumothorax, one infarction of the spleen (which regressed spontaneously) and one peroperative bleeding, which did not require transfusion. A complication occurred in four patients in group II (8.3%): one peritoneal hematoma (which required reoperation and transfusion), two peroperative bleedings without the need for transfusion and one capsular effraction. These complications are listed in Table 3.

There was no mortality. Mean operative time was 131 min in group I (58–300 min) and 129 min in group II (65–240 min). The average length of hospital stay was 5.6 days (3–15 days) in group I and 5.1 days (3–12 days) in group II. The endocrinopathy was successfully cured in all patients with functioning tumors. Results in the two groups of patients are compared in Table 4.

Discussion

There are few absolute contraindications for LA [4, 5]. Some contraindications, such as major coagulation disorders, are not specific to adrenal surgery. Previous surgery in the adrenal area may be a contraindication, depending on the experience of the operator, e.g., partial or total nephrectomy, hepatic resection on the right side, distal pancreatectomy or splenectomy on the left side. Most of the other contraindications are related to the adrenal tumor itself. Invasive adrenal carcinoma is certainly an absolute contraindication for a laparoscopic approach. Malignancy can be demonstrated by extra-adrenal invasion. This emphasizes the need for a complete preoperative investigation using imaging techniques.

In our experience, a 12-cm or larger tumor is also a contraindication. The working space available is limited, particularly on the right side. The dissection is time consuming. The largest tumor that we have resected was an 11-cm myelolipoma on the left side. As in open surgery, large tumors should be excised en bloc. During the laparoscopic procedure, there is a major risk of capsular effraction. We encountered one capsular effraction during the dissection of a 75-mm left pheochromocytoma. We did not perform open surgery, because the capsular effraction was minimal; however, the need for such caution is questionable. We think that tumors larger than 6 cm in diameter can only be removed laparoscopically by surgeons experienced in this technique. There is still no consensus concerning potentially malignant adrenal tumors [4, 6].

Tumor size is usually considered an indicator of malignancy [7, 8, 9]. Tumors larger than 6 cm in diameter are likely to be malignant. Nevertheless, one must admit that many adrenal adenomas are larger than 6 cm. However, some potentially curable adreno-cortical carcinomas are small. Therefore, for some authors, the size is not an indicator of malignancy [10].

CT and MRI are certainly useful to separate adrenal adenomas from nonadenomatous lesions. Heterogeneous adrenal tumors with an irregular configuration are likely to be malignant, regardless of size. Unenhanced CT attenuation values under 10 Hounsfield units (HU) and 1-h post-contrast attenuation values under 30 HU are indicators of benign lesions. Most adrenal adenomas and all myelolipomas have a lipid-rich composition (demonstrated by MRI) compared with the lipid-depleted nature of the majority of nonadenomatous lesions. Adrenal scintigraphy with ^{131}I NP-59 also has a significant role. An increased tracer uptake by a non-hyperfunctioning lesion indicates that the lesion is probably benign [11]. Preliminary results with positron emission tomography seem promising but should be confirmed by other studies.

Even if it is unilateral, an incidentally discovered adrenal mass can also be a secondary tumor. In cases where a secondary tumor is suspected, fine needle aspiration (FNA) can be recommended. With experienced cytopathologists, FNA is certainly the most effective method for confirming metastatic disease. Nevertheless, review of the literature suggests that malignancy cannot be ruled out in all cases on the basis of preoperative investigations, such as CT, MRI, NP-59 and FNA. In addition, FNA is an invasive method with a low but appreciable

rate of complications, including pneumothorax and bleeding.

Thus, one must admit that, in some cases, diagnosis of malignancy will be established during or after surgery. In these cases, laparoscopy should be considered as an additional procedure of investigation to assess the possible malignancy of a tumor. The decision to remove the tumor laparoscopically or to perform open surgery will be based on this final peroperative evaluation.

In this study, in 48 of the 150 LAs (32%), the adrenal tumor was considered to be potentially malignant. Should LA be proposed in these 48 patients? Malignancy was observed in six cases (12.5%). In two of the three primary malignant tumors, malignancy was not suspected during surgery, and the tumors were completely removed laparoscopically without any difficulties. Retrospectively, we do not think that we would have performed more extensive surgery using an open approach. In the third case, an adreno-cortical carcinoma was strongly suspected at the start of the procedure because of the macroscopic features of the tumor. We immediately switched to an open, extensive procedure. In the three other cases, diagnosis of adrenal metastasis was strongly suspected preoperatively. Malignancy was confirmed at the beginning of the procedure. In two cases, an open operation was performed because of difficulties of dissection and bleeding, but in one case, the tumor was completely and easily removed laparoscopically. In this last case, we would not have performed a different operation using an open approach. Therefore, we think that LA should be considered for the few patients with a solitary adrenal metastasis in whom surgery is indicated [12, 13].

The rate of complications was similar in the two groups: 7.8% in group I and 8.3% in group II. Complications in group II were essentially related to difficulties of dissection. Most of the complications in group I were observed in the first patients of our series, probably due to our lack of experience with LA [3, 4].

The rate of conversion is also similar in the two groups. However, the reasons for conversion are different. In group I, conversions were used because of difficulties of dissection. In group II, the three conversions were related to suspected malignancy during operation.

Paradoxally, the mean operative time was almost the same in the two groups: 131 min in group I and 129 min in group II. With our experience increasing, it seems to us that large benign tumors (6–8 cm) that involve the whole gland are sometimes easier to dissect from surrounding structures than small tumors, which require the dissection of the gland itself.

Conclusion

In our opinion, LA can be proposed for large tumors or tumors at risk for malignancy. The risk of malignancy should be evaluated at the start of the laparoscopic procedure. If local invasion is observed or if there is a strong suspicion of malignancy, open surgery should be performed. Although most patients with adrenal metastases are not candidates for surgery, LA can be proposed to remove a solitary adrenal metastasis in the few patients in which a primary carcinoma has already been completely resected during a previous operation.

LA should not be opposed to open surgery. The two procedures can be complementary as, in some cases, LA may be considered as an additional method of exploration for tumors at risk of malignancy.

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