

# Applicability of Laparoscopic Adrenalectomy in a Prospective Study in 150 Consecutive Patients

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**Hypothesis:** Within a decade, laparoscopic adrenalectomy has become the new “gold standard” for the surgical treatment of most adrenal lesions. Designed as a single-center project focused on patients with adrenal lesions, this study should provide an indication of the number of patients requiring surgery who can safely undergo laparoscopy, after consideration of such selection criteria as tumor size and benign or malignant lesion status at magnetic resonance imaging. Furthermore, the access-related complications were analyzed.

**Design:** According to a prospective protocol, 150 consecutive patients selected for adrenal surgery were assigned to transperitoneal endoscopic or open adrenalectomy.

**Setting:** University hospital section of endocrine surgery.

**Results:** One hundred two patients (68%) were selected for a laparoscopic approach that had to be con-

verted to open surgery in 5 patients (5%). Two malignant cortisol-secreting lesions were operated on laparoscopically because of their small size and benign appearance at magnetic resonance imaging. During histological examination, 14 (29%) of 48 patients assigned to transperitoneal open adrenalectomy had lesions deemed malignant (16 [11%] of 150 patients). The laparoscopic group had significantly fewer complications (9%) than did the open group (21%;  $P = .04$ ).

**Conclusions:** By applying defined selection criteria for the treatment of adrenal lesions, transperitoneal endoscopic adrenalectomy can be a safe procedure and may be performed in at least two thirds of patients. The choice of endoscopic or open approach in larger tumors should depend on the results of preoperative imaging studies and the endocrine surgeon's experience in endoscopic adrenal surgery.

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**A** COMPREHENSIVE LITERATURE search did not reveal any record of randomized trials comparing open with endoscopic adrenalectomy. It is, however, well documented in several studies that an endoscopic approach has advantages over the open one, if performed by an experienced team.<sup>1-5</sup> Because of the advantages, which include decreased postoperative pain, reduced time to return of bowel function, decreased length of hospitalization, and the potential for earlier return to normal life, many authors proclaim the endoscopic approach the new “gold standard” for the treatment of benign adrenal lesions smaller than 60 mm.<sup>6,7</sup> Because of the apparent advantage of laparoscopic adrenalectomy,<sup>8</sup> prospective studies will no longer be performed in which patients are randomized between endoscopic and open procedures.

Taking into account the size of the adrenal lesions, biochemical findings, and the

results of preoperative imaging studies predicting the status of these lesions,<sup>9</sup> we designed a prospective protocol.<sup>10</sup> Conducted in a single center, results of this study should provide an indication of the number of patients awaiting surgery who can safely undergo laparoscopic adrenalectomy, on the basis of clear selection criteria, without any malignant lesions being overlooked. Furthermore, the access-related complications were also analyzed.

## METHODS

All patients with adrenal lesions selected for surgery were enrolled in this prospective 5-year study. The study group consisted of 150 consecutive patients (99 women, 51 men), with a mean  $\pm$  SD age of  $51 \pm 13.9$  years (range, 20-79) with a total of 158 adrenal lesions.

## STUDY DESIGN

Routine preoperative evaluation for hormonal activity included screening for phoe-

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**Table 1. Preoperative Biochemical Findings in 150 Consecutive Patients\***

| Indication                               | Group 1: Laparoscopic Approach |                         | Group 2: Open Approach |                         |
|--|--------------------------------|-------------------------|------------------------|-------------------------|
|  | No. of Patients                | No. of Malignant Tumors | No. of Patients        | No. of Malignant Tumors |
| Conn syndrome                            | 38 (25.3)                      | 0                       | 1 (0.7)                | 0                       |
| Pheochromocytoma                         | 26 (17.3)                      | 0                       | 14 (9.3)               | 2                       |
| Nonfunctioning adenoma                   | 15 (10.0)                      | 0                       | 16 (10.7)              | 7                       |
| Cushing syndrome                         | 15 (10.0)                      | 2                       | 5 (3.3)                | 1                       |
| Corticotropin-dependent Cushing syndrome | 3 (2.0)                        | 0                       | 4 (2.7)                | 0                       |
| Other tumors                             | 5 (3.3)                        | 0                       | 8 (5.3)                | 4                       |
| <b>Total</b>                             | <b>102 (68.0)</b>              | <b>2</b>                | <b>48 (32.0)</b>       | <b>14</b>               |

\*Data in parentheses are percentages.

chromocytoma, hyperaldosteronism, hypercortisolism, and virilizing or feminizing tumors.<sup>11</sup> Standard preoperative evaluation included gadolinium-enhanced magnetic resonance (MR) imaging with chemical shift imaging as described recently to predict the benign or malignant status and size of the lesion.<sup>9</sup> Particular attention was given to tumor size on MR images, infiltration of adjacent organs or structures, tumor thrombus in the inferior caval or renal vein, and distant metastases. Furthermore, the morphology of the contralateral gland and the gadolinium enhancement and fat content of the lesion itself were evaluated to plan for the most appropriate surgical access. Informed consent was obtained from all patients participating in this study, and those assigned to the laparoscopic group were free to choose the open access method.

#### SURGICAL PROTOCOL

Hormonally active or inactive tumors 60 mm or smaller (size determination according to preoperative MR images) that were benign in appearance on MR images were surgically removed by using a transperitoneal laparoscopic flank approach with the patient in the lateral decubitus position (group 1). Dissection was performed with harmonic scalpel, hook cautery, and electrocoagulating scissors. All tumors were extracted in their entirety, along with the adrenal gland and the surrounding fatty and lymphatic tissue. They were collected in a plastic bag to allow detailed histomorphological classification. Wherever tumors revealed an apparent malignancy or were larger than 60 mm, an open anterior approach (group 2) was selected as the most appropriate surgical procedure.

All specimens were histopathologically examined after surgical resection. In cases of malignancy, specimens were classified according to the criteria proposed by Aubert et al.<sup>12</sup> All patients were monitored, both clinically and biochemically, within a mean  $\pm$  SD of 37  $\pm$  17 months (range, 6-66 months).

All data were entered into an electronic database, and statistical analysis was performed (SPSS r11.0.1; SPSS Inc, Chicago, Ill). For comparison of groups, we used the *t* test and Mann-Whitney test where appropriate. Differences were considered statistically significant for *P* < .05.

## RESULTS

### GROUP 1: TRANSPERITONEAL ENDOSCOPIC APPROACH

One hundred two patients (68%) with a total of 106 adrenal lesions were selected for laparoscopic adrenalectomy. The preoperative biochemical findings are summarized in **Table 1**. The endoscopic approach was successful in 97 patients (95%). In 5 patients, however, the ap-

proach had to be converted because of 3 cases of bleeding from the inferior caval vein (30, 50, and 55 mm), 1 tumor adhesion (20 mm), and 1 tumor rupture (40 mm).

Histological examination revealed 2 malignant cortisol-producing lesions (25 and 50 mm in diameter) in 2 patients, although neither required reoperation and continued to be free from disease 27 and 60 months later, respectively. All other lesions were benign at histopathological examination. Bilateral endoscopic adrenalectomy was performed in 4 patients owing to 3 cases of corticotropin-dependent Cushing syndrome and 1 case of bilateral pheochromocytoma in multiple endocrine neoplasia type 2A.

As a result of growing experience, as well as of the excellent results achieved in the prediction of the benign or malignant status of the lesions with MR imaging, it was possible to operate on 9 tumors larger than 60 mm by using the laparoscopic approach during the last 15 months of the study; there were 5 cases of pheochromocytoma (61, 62, 65, 70, and 90 mm), 3 cases of benign nonfunctioning adenoma (65, 65, and 70 mm), and 1 ganglioneuroma (100 mm).

### GROUP 2: TRANSPERITONEAL OPEN APPROACH

With use of the established protocol, 36 patients with a total of 40 adrenal lesions were selected for the open transperitoneal approach. Bilateral adrenalectomy was performed in 4 of these patients because of corticotropin-dependent Cushing syndrome (*n*=3) and bilateral pheochromocytoma in multiple endocrine neoplasia type 2A (*n*=1). Moreover, these 4 patients were excluded from the endoscopic approach owing to their poor general condition (*n*=2), neuroendocrine pancreatic cancer with concomitant pancreatic resection (*n*=1), or concomitant aortic tube graft because of aneurysm (*n*=1).

An additional 12 tumors smaller than 60 mm were added to this group because of patient choice in 5 cases, 3 concomitant operations (2 aortic aneurysm repairs and 1 intestinal reconstruction), 3 ectopic localizations because of extra-adrenal pheochromocytoma, and severe bone manifestation of pituitary-dependent hyperadrenocorticism in 1 case. The preoperative biochemical findings are summarized in **Table 1**.

Histological examination revealed 14 malignant tumors (**Table 2**), 4 of which were metastases from the lung (*n*=2), colon (*n*=1), or hypernephroma (*n*=1). Two

additional malignant lesions, 1 pheochromocytoma and 1 paraganglioma, were catecholamine secreting. Histopathological examination revealed malignancies in 1 patient with a cortisol-producing lesion and 7 patients with nonfunctioning tumors.

### TUMOR SIZE AND MALIGNANCY

Histological examination was used to confirm tumor size and malignancy. One hundred forty-two lesions were classified as benign and 16 as malignant. 124 (78%) lesions were smaller than 60 mm and 34 (22%) larger than 60 mm, 25 (18%) of 142 benign lesions were larger than 60 mm, 6 (38%) of 16 malignant tumors were smaller than 60 mm (ie, 5% of all lesions smaller than 60 mm), 10 (63%) of 16 malignant lesions were larger than 60 mm, and 10 (29%) of 35 tumors larger than 60 mm were classified malignant.

**Table 2. Tumor Characteristics**

| Characteristic           | Group 1:<br>Laparoscopic Approach | Group 2:<br>Open Approach |
|--------------------------|-----------------------------------|---------------------------|
| No. of patients          | 102 (68%)                         | 48 (32%)                  |
| No. of tumors            | 106                               | 52                        |
| Mean tumor diameter, mm* | 38 (3-100)                        | 68 (20-160)               |
| No. of benign tumors     | 104                               | 38†                       |
| No. of malignant tumors  |                                   |                           |
| Adrenocortical carcinoma | 2‡                                | 8                         |
| Metastasis               | 0                                 | 4                         |
| Pheochromocytoma         | 0                                 | 1                         |
| Paraganglioma            | 0                                 | 1                         |

\*Data in parentheses are the range.

†Includes 7 paragangliomas.

‡Diameters were 25 and 50 mm.

### COMPLICATIONS AND LONG-TERM FOLLOW-UP

Complications occurred in 9 patients (9%) from group 1: conversion to the open approach (n=5), blood transfusion (n=2), hematoma at the lower pole of the left kidney (n=1), and incisional hernia (n=1). In group 2, complications arose in 10 patients (21%): blood transfusion (n=3), wound infection (n=2), incisional hernia (n=2), hematoma (n=1), severe postoperative paralysis of the bowels (n=1), and deep vein thrombosis (n=1). The complication rate in the laparoscopic group was significantly lower than that in the open group (Mann-Whitney test,  $P=.04$ ). During long-term follow-up, no recurrence was observed in patients with benign tumors. Details of follow-up in patients with malignant lesions are summarized in **Table 3**.

### COMMENT

If tumor size ( $\leq 60$  mm) and the results of preoperative imaging were taken into consideration, 111 lesions (70%) would have been considered optimal for an endoscopic approach. In our extensive prospective single-center study, 101 (64%) tumors were extracted with a laparoscopic approach. Five patients preferred to undergo open surgery, and surgery in 5 (5%) patients had to be converted.

For endoscopic removal of adrenal lesions, several routes have been described.<sup>10</sup> To our knowledge, no study results demonstrate a consistent benefit of adopting one of the available endoscopic approaches, transperitoneal or retroperitoneal, over another.<sup>13</sup>

Transperitoneal laparoscopic adrenalectomy offers intra-abdominal landmarks. In addition, open surgery allows exploration of the abdominal cavity, and, in some cases, treatment of concomitant intra-abdominal dis-

**Table 3. Detail and Follow-up in Malignant Lesions**

| Patient No./<br>Sex/Age, y | Adrenal Disease            | Side | Size, mm | Status*   | Surgical Approach† | Follow-up Result       | No. of<br>Follow-up Months |
|----------------------------|----------------------------|------|----------|-----------|--------------------|------------------------|----------------------------|
| 13/F/32                    | Adrenocortical carcinoma‡  | R    | 50       | Benign    | Laparoscopic       | Free of disease        | 60                         |
| 115/F/30                   | Adrenocortical carcinoma‡  | L    | 25       | Benign    | Laparoscopic       | Free of disease        | 27                         |
| 18/M/51                    | Metastasis (lung cancer)   | R    | 40       | Malignant | Open               | Free of disease        | 42                         |
| 21/F/57                    | Metastasis (hypernephroma) | R    | 35       | Malignant | Open               | Progression of disease | 40                         |
| 92/F/51                    | Metastasis (lung cancer)   | R    | 50       | Malignant | Open               | Refused follow-up      | NA                         |
| 103/M/57                   | Metastasis (colon cancer)  | L    | 82       | Malignant | Open               | Died§                  | 14                         |
| 28/F/42                    | Adrenocortical carcinoma   | L    | 160      | Malignant | Open               | Free of disease        | 35                         |
| 29/F/57                    | Adrenocortical carcinoma   | R    | 58       | Malignant | Open               | Refused follow-up      | NA                         |
| 57/F/43                    | Adrenocortical carcinoma   | L    | 75       | Malignant | Open               | Free of disease        | 34                         |
| 85/F/74                    | Adrenocortical carcinoma   | R    | 90       | Malignant | Open               | Died                   | 10                         |
| 86/M/47                    | Adrenocortical carcinoma   | R    | 180      | Malignant | Open               | Died                   | 18                         |
| 112/M/34                   | Adrenocortical carcinoma   | L    | 170      | Malignant | Open               | Local recurrence       | 15                         |
| 126/F/24                   | Adrenocortical carcinoma   | L    | 110      | Malignant | Open               | Died                   | 7                          |
| 149/M/62                   | Adrenocortical carcinoma‡  | L    | 130      | Malignant | Open               | Free of disease        | 6                          |
| 117/F/61                   | Paraganglioma              | R    | 70       | Malignant | Open               | Free of disease        | 11                         |
| 22/F/42                    | Pheochromocytoma           | R    | 90       | Benign    | Open               | Free of disease        | 48                         |

Abbreviations: L, left; NA, not applicable; R, right.

\*Lesion status assessed at magnetic resonance imaging.

†Laparoscopic adrenalectomy was performed with a lateral approach and open adrenalectomy with an anterior approach.

‡Malignant cortisol-secreting tumor in a patient with Cushing syndrome.

§Died of colon cancer.

||Died of adrenocortical carcinoma.

ease.<sup>10</sup> From our ongoing experience, a clear exposure makes removal of larger adrenal lesions possible<sup>14</sup> as demonstrated in 9 patients in this study. One obvious disadvantage of the transabdominal route is the need to reposition the patient for bilateral adrenalectomy, as with 4 of the patients in our study. Potential risks include injury of intra-abdominal organs and dissection problems due to adhesions from previous surgery. These risks were, however, not encountered in our study.

Hormonally inactive and active tumors, including pheochromocytoma, as demonstrated in 27 lesions, can be removed with the same success rate. The 5% conversion rate in the patients in our study is in accordance with findings in the literature, as well as findings with extra-peritoneal techniques.<sup>15</sup> The prevalence of primary adrenocortical carcinoma is clearly related to the size of the lesion. Adrenocortical carcinoma accounts for 2% of tumors 40 mm or smaller, 6% of tumors from 41 to 60 mm, and 25% of lesions larger than 60 mm.<sup>16</sup> In our study, 29% of all tumors larger than 60 mm were classified malignant; on the other hand, 38% of all malignant lesions were smaller than 60 mm. During histopathological examination, 71% of all tumors larger than 60 mm were classified benign. Therefore, merely considering size when choosing surgical access would lead to endoscopic removal of 38% of adrenal malignant tumors.

Imaging techniques such as unenhanced computed tomography or gadolinium-enhanced MR imaging with chemical shift imaging are capable of characterizing adrenal lesions in as many as 95% of cases.<sup>9</sup> Tumors larger than 60 mm classified as benign at preoperative imaging may be removed laparoscopically.

At present, relative contraindications to laparoscopic adrenalectomy are a definitive or assumed diagnosis of invasive adrenocortical carcinoma. All but 2 malignant tumors were surgically resected by using an open approach, thus underlining the importance of open techniques for suspected malignancy, even in this era of advanced endoscopic adrenal surgery. The 2 small (25-mm and 50-mm) cortisol-secreting tumors were considered benign at preoperative imaging and were subsequently removed laparoscopically. Neither patient required reoperation, and both were free from disease after 27 and 60 months.

Nine percent of patients with laparoscopic adrenalectomy and 21% with open adrenalectomy had complications. These findings demonstrate a significantly lower rate of adrenalectomy-related complications during or after laparoscopic surgery, which is in accordance with findings in a recently published meta-analysis.<sup>8</sup> Transperitoneal endoscopic adrenalectomy is a safe procedure in adrenal tumors as large as 60 mm displaying a benign appearance and may be used in at least two thirds of patients requiring surgery.

Choosing an endoscopic or an open approach in larger tumors depends on the results of preoperative imaging and the endocrine surgeon's experience with endoscopic adrenal surgery.<sup>14,17</sup> Although the patients in this study were not randomized to a particular approach, the significantly lower access-related morbidity of the endoscopic group makes this approach favorable as the new gold standard as long as well-defined criteria are used.

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