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Laparoscopic approach in the treatment of malignant adrenal tumours

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ABSTRACT

Introduction: Malignant primary or secondary adrenal tumours are uncommon. For most of them early surgery with adrenalectomy is the only means of cure. Although controversy exists on this issue, the increasing experience in laparoscopic surgery extends the indication for laparoscopic adrenalectomy to potentially malignant and to metastatic adrenal tumours. Our aim was to evaluate the technical feasibility of laparoscopic adrenalectomy for malignant neoplasias, describing the results of our consecutive series of patients.
Material and methods: We retrospectively analysed 13 patients who underwent laparoscopic adrenalectomy for malignant neoplasia between March 1999 and June 2009 at the Hospital de Clínicas at the University of Buenos Aires and at the Hospital Alemán in Buenos Aires. A transperitoneal laparoscopic approach was used in all patients. The mean follow-up time was 37.9 months (2-84).
Results: Thirteen laparoscopic adrenalectomies were performed due to malignant neoplasia. Mean age was 55.2±12 years. The male to female ratio was 10:3. Five patients had an adrenal carcinoma, one patient a malignant phaeochromocytoma, and 7 patients had metastatic tumours. Three patients required conversion to laparotomy. Average operation time was 146.4 min. There were two perioperative complications and no mortalities. Average length of hospital stay was 4.6 days (1-35). The survival at 3 years was 46%. The cause of death was the underlying disease in all cases.
Conclusion: Laparoscopic adrenalectomy is a reasonable technique for malignant adrenal tumours, when the open oncological resection can be reproduced by the laparoscopic approach.

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Abordaje laparoscópico en el tratamiento de las tumoraciones adrenales malignas

Palabras clave:
Suprarrenalectomía laparoscópica
Tumores malignos suprarrenales
Carcinoma corticosuprarrenal

R E S U M E N

Introducción: Los tumores suprarrenales malignos son infrecuentes. La cirugía es el tratamiento que ofrece mejores resultados. Aunque existe controversia al respecto, la creciente experiencia en cirugía laparoscópica permitió la indicación de suprarrenalectomías laparoscópicas en tumores primarios potencialmente malignos y metastásicos. Nuestro objetivo es evaluar la factibilidad técnica de la suprarrenalectomía laparoscópica en neoplasias malignas y describir los resultados de nuestra serie consecutiva de pacientes.

Material y métodos: Se analizaron retrospectivamente 13 pacientes (10 varones y 3 mujeres) operados por neoplasias suprarrenales primarias y secundarias por vía laparoscópica entre marzo de 1999 y junio de 2009 en el Hospital de Clínicas de la Universidad de Buenos Aires y en el Hospital Alemán de Buenos Aires. El abordaje transperitoneal se utilizó en todos los casos. El seguimiento promedio fue de 37,9 meses (2-84).

Resultados: Se operaron 13 pacientes que tenían neoplasias malignas suprarrenales por vía laparoscópica. La edad promedio fue de 55,2 ± 12 años, con una relación hombre/mujer de 10/3. Cinco pacientes presentaron carcinomas corticosuprarrenales, uno presentó feocromocitoma maligno y 7 presentaron tumores metastásicos. Tres pacientes requirieron conversión a cirugía abierta. El tiempo operatorio promedio fue de 146,4 min. Se presentaron 2 complicaciones postoperatorias. No hubo mortalidad perioperatoria en la serie. La estadía hospitalaria promedio fue de 4,6 días (1-35). La sobrevida actuarial a 3 años fue del 46%. La causa de muerte en todos los casos fue la enfermedad de base.

Conclusiones: El abordaje laparoscópico es razonable para los tumores suprarrenales malignos cuando se puede reproducir la técnica oncológica realizada por vía abierta.

Introduction

Since the first successful adrenalectomies were performed in 1926 by César Roux[1] in Switzerland and by Charles Mayo[1] in the United States, significant advances have occurred leading to the development of the minimally invasive techniques described by Joseph Petelin[2] and Michael Gagner[3] in 1992. Since then, laparoscopic adrenalectomy has become the approach of choice for most benign neoplasms of the adrenal gland. Due to increasing experience in laparoscopic surgery, some centres have extended the indication for laparoscopic adrenalectomy to include potentially malignant adrenal tumours and adrenal metastases.[4,5] However, many endocrine surgeons have rejected laparoscopy as an appropriate approach route for malignant or potentially malignant diseases[3] due to the size of the tumour, the possibility of inadequate resection and the potential increase in recurrence in the ports of entry or in the bed of the lesion, and because of case reports describing locoregional or distant recurrences.

Articles in international medical literature are few and contain a small number of patients.

The aim of this study is to evaluate the technical feasibility of laparoscopic adrenalectomy for suspected and unsuspected malignant neoplasms in the preoperative period, and evaluate oncological outcomes.

Material and methods

A retrospective review was performed of the medical records of patients who underwent laparoscopic surgery for adrenal tumours between March and June 2009 at José de San Martín Hospital, University of Buenos Aires and the Hospital Alemán in Buenos Aires.

Included patients had primary or secondary malignant neoplasms which were either suspected or unsuspected in the preoperative period, with an indication for surgical treatment. Those excluded were patients with tumours larger than 10 cm, imaging evidence of invasion of adjacent organs and patients with functioning primary tumours with long-distance metastasis.

Of the 145 laparoscopic adrenalectomies, 132 patients (91%) were excluded because of having benign tumours and the 13 remaining patients were included.

All patients underwent complete preoperative staging (laboratory, ultrasound and CT). MRI was performed in 2 cases (one case of primitive pulmonary adrenal metastasis and another case of primitive renal metastasis).

In the 7 patients under oncological observation due to extra-adrenal neoplasms with metastatic tumours, suspected because of abnormal enlargement of the adrenal gland on the CT, the diagnosis was confirmed by fine needle aspiration biopsy.

The patients with primitive adrenal tumours underwent endocrine assessment to define the functional pattern (urinary catecholamines, aldosterone and plasma renin, potassaemia, cortisol cycle, urinary free cortisol, testosterone, delta 4 androstenedione and S-DHA).

The medical records, preoperative imaging tests, surgical procedures and findings, pathology reports (final diagnosis and margins), complications, postoperative outcome and follow-up were all reviewed. The variables studied were age, sex, tumour size and weight, operative time, morbidity, hospital stay, conversions, and oncological outcomes.

Results

During the study period 13 patients with malignant adrenal tumours underwent laparoscopic procedures. Table 1 describes the patient and tumour characteristics.

The five cases of adrenocortical carcinoma were presented clinically as Cushing's syndrome, abdominal pain and incidentaloma in 3 cases. Phaeochromocytoma presented with a clinical profile of hypertension and headaches. The 7 metastatic tumours were diagnosed in oncological tests for their underlying disease.

The lateral transperitoneal laparoscopic approach was used in 13 patients. There were 3 conversions to open surgery (23%): a malignant phaeochromocytoma case due to fibrous adhesions and haemorrhage, a case of metastatic lung cancer due to technical difficulties with the laparoscopic instruments and an adrenocortical carcinoma case due to haemorrhaging from the right upper pole artery.

Table 2 describes the operating data and surgical series.

The pathology report found that the resection margins were tumour-free in all surgical specimens. According to the MacFarlane classification modified by Sullivan, all adrenocortical carcinomas corresponded to stage 2.

Postoperative complications included acute urinary retention after prolonged surgery in one case of primary adrenal metastasis from the lung, and an *Acinetobacter baumanii* wound infection in a patient with adrenocortical carcinoma.

The average follow-up time for the patients was 37.9 months (2-84). Of the 5 cases of adrenal carcinoma, 4 were disease-free at 84, 81, 77, and 32 months after surgery; the fifth died after the 8th postoperative month with a disease-free survival of three months. The patient with malignant phaeochromocytoma died in the first postoperative year and had a disease-free period of five months. The five lung cancer patients had an average survival of 26 months (2-37) after adrenalectomy. Of the metastatic renal tumour patients, one is disease-free 58 months after surgery and the other is also disease-free at 11 months. The cause of death was the underlying disease in all cases. Survival at 3 years was 46% (Table 3 and Figure). The average survival of the primary tumour patients was 49 months and that for the secondary tumour patients was 28 months. As of June 1, 2009, six patients were alive with no signs of the disease.

Discussion

The role of laparoscopy in malignant neoplasms of the adrenal gland is controversial. Due to there being few reported cases

Table 1 – Patient and tumour characteristics

	Laparoscopic adrenalectomy (n=13)
Age	55.2 (37-72)
Sex	
Male	10
Female	3
Side	
Right	6
Left	7
Primary tumours	6 (46%)
Adrenocortical carcinoma	5
Malignant phaeochromocytoma	1
Metastatic tumour	7 (54%)
Lung	5
Kidney	2
Tumour size, cm	6.1 (2.8-8.2)
Primary tumours	7.04 (6-8.2)
Metastatic tumours	5.4 (4-8)
Tumour weight, g	122.9 (18-255)

Table 2 – Operative and perioperative data

	Laparoscopic adrenalectomy (n=13)
Operating time, min	146.4 (50-255)
Patients who required a transfusion during the operation (%)	2 (15)
Conversions, n (%)	3 (23)
Complications, n (%)	2 (15)
Mortality, n (%)	0 (0)
Hospital stay, days	4.6 (1-35)

Table 3 – Oncology results

	Laparoscopic adrenalectomy (n=13)
Follow-up, months	37.9 (2-84)
Disease-free survival, months	31.4 (1-84)
Actuarial survival at 3 years, %	46
Living without evidence of disease, n (%)	6 (46.1)
Death due to disease, n (%)	7 (53.9)

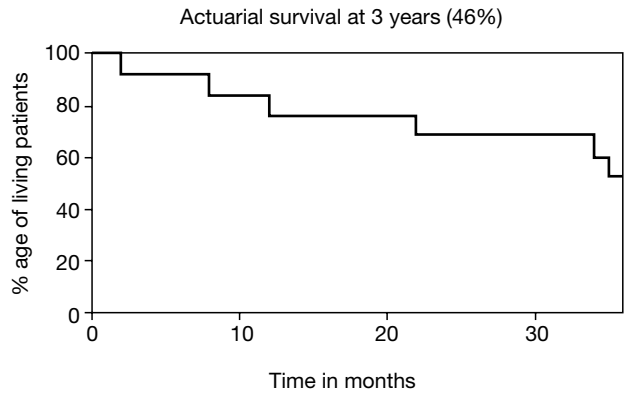

Figure – Actuarial survival at 3 years (46%).

in the literature, and also due to the contradictory nature of their findings, no consensus has been reached on the standard of care. The debate focuses on the following: 1) the technical feasibility of achieving oncological resection equal to those in open surgery, and 2) the risk of the tumour spreading by the pneumoperitoneum and the possibility of neoplastic implants at trocar sites. The above two arguments, based on early studies of laparoscopic colectomy due to cancer, have now been discarded.[1]

In connection with adrenal tumours, potential spreading due to pneumoperitoneum and neoplastic implants at the trocar sites has not been shown to be a cause of future relapses. However, tumour manipulation with capsular effraction or tumour morcellation has been associated with both benign and malignant disease recurrence. It is for this last reason that tumour size plays a decisive role in the surgical approach to use. [6,7] Even for benign conditions, technical precautions are taken in all surgeries to prevent capsular rupture of the tumour, such as using a nylon bag to extract the piece and evacuating the pneumoperitoneum with the trocars in position. There were no recurrences attributable to the procedure in our series (implantation in trocar entry holes or carcinomatosis).

What are the primary malignant tumours of the adrenal gland for which laparoscopic treatment is indicated? This is a difficult question to answer. Only invasion of adjacent organs and metastasis indicate malignancy. Unfortunately, preoperative imaging studies do not accurately show the potential malignancy of adrenal neoplasms. Even though CT, the technique of choice for the adrenal glands, may show heterogeneity and irregular margins, and the MRI may show T2 signal hyperintensity, none of these studies can prove a lesion to be malignant when there are no obvious signs of compromised adjacent structures or metastasis. Tumour size has been used by some researchers to predict malignancy, but there is no consensus at present.

One possible answer to this question is that all adrenal tumours should be addressed laparoscopically, as otherwise open surgery would be performed on a large percentage of benign lesions because of the mere suspicion of malignancy. When faced with the discovery of large tumours, which are difficult to treat laparoscopically, or where the invasion of adjacent structures or other obvious signs of malignancy is noted, conversion to open surgery is required. On the other hand, there are tumours that can be resected laparoscopically while observing all the principles of conventional surgery. It is in these latter cases where the unexpected diagnosis of malignancy is obtained post-operatively.[8]

The currently recognised contraindications for laparoscopic adrenalectomy are tumours larger than 10-12 cm, significant peritumoral adhesions, invasion of adjacent structures, lymphadenopathy and evidence of metastatic disease.[6,17]

Kendrick et al[9] analysed a series of 58 patients with adrenocortical carcinoma treated surgically. Four patients with difficult laparoscopic resections in tumours smaller than 7 cm had abdominal carcinomatosis secondary to tumour morcellation. They conclude that small non-invasive tumours are amenable to laparoscopic resection, although they note the lack of studies to support this. Bulky tumours that are difficult to treat during the operation, or those with local invasion, are indications for open surgery and support the fundamental premise that the first surgery is the most important in the treatment of these tumours, and that violation of oncological surgical principles is unacceptable.

Meanwhile, Kebebew et al,[10] after evaluating 23 laparoscopic adrenalectomies for adrenal tumours (6 primary and 17 metastatic), conclude that the laparoscopic approach is acceptable for malignant tumours when complete resection is technically feasible in cases without local invasion. However, there was a high rate of local recurrence, and the authors did not make it clear if these results could have been improved by using conventional approaches.

Similarly, Henry et al,[11] after analysing a series of 19 laparoscopic adrenalectomies, conclude that it is a safe procedure for potentially malignant tumours, although they recommend conversion to open surgery when faced with intraoperative difficulties or evidence of malignancy.

McCauley and Nguyen[12] carried out a review and analysed 11 series of patients undergoing laparoscopic procedures for primary malignant adrenal tumours between 2002 and 2007. There was a total of 48 patients, of whom 19 (40%) had disease recurrence (12 with local recurrence, 25%). The highest average survival reported in these series was 47 months in the study by Henry et al[11] and 45 months for patients in the Ramacciato et al[13] study. None of the 48 patients had metastases at the trocar sites and 5 patients (10.4%, all from the Gonzalez et al series[14]) had peritoneal recurrence. The average tumour size in the 48 patients was 8.5 cm (Table 4). The authors of this review consider, therefore, that tumours larger than 9 cm or those with signs of local invasion would benefit from a conventional approach to achieve better exposure and prevent tumour rupture.

Table 4 – Series of laparoscopic adrenalectomies due to primary malignant tumours between 2002 and 2009

Author	Primary malignant tumours, n	Average tumour size, cm	Follow-up, months	MTS peritoneal/ trocars	Recurrence	Disease-free living patients, n (%)
Henry, 2002	6 ACC	7.4	47	0	1 distance	5 (83)
Porpiglia, 2004	6 ACC	6.9	30	0	0	5 (83)
Corcione, 2005	2 ACC	8.5	13.6	0	1 local	1 (50)
González, 2005	6 ACC	5.3	28	5 P	6 local and distance	0 (0)
Gill, 2005	6 ACC 1 MP	5	26	0	2 local 1 distance	3 (43)
Palazzo, 2006	3 ACC	6.8	34	0	1 distance	2 (66)
Lombardi, 2006	4 ACC 3 MP	5.9	23	0	1 local 1 distance	4 (57)
Liao, 2006	4 ACC	6.2	39	0	1 local and distance	1 (25)
Schlamp, 2007	1 ACC	7.5	4	0	Local	1 (100)
Ramacciato, 2007	2 ACC	8.5	45	0	0	2 (100)
Nocca, 2007	4 ACC	8.5	34	0	1 distance	3 (75)
Mezzadri, 2009	5 ACC 1 MP	7.04	38	0	1 local 1 distance	4 (66)

ACC indicates adrenocortical carcinoma; MP, malignant phaeochromocytoma; MTS, metastasis; P, peritoneal.

As for secondary tumours in the adrenal gland, numerous researchers agreed that resection of isolated metastases provides better long-term survival than other treatments do, especially when compared with early kidney or non-small cell lung carcinomas. Luketich et al[15] established selection criteria for metastasectomy: 1) complete control of the primary tumour, 2) comprehensive staging showing that this is an isolated metastasis, and 3) patient's ability to tolerate general anaesthesia.[5,6,16] The 6 cases in this series met these selection criteria. One patient with lung cancer died due to local and systemic progression of the disease. None of the others had recurrence in the bed.

As in all studies published to date, our series of 13 patients does not allow us to draw statistically significant conclusions due to the small number of cases, but we have made some observations. We believe that laparoscopic adrenalectomy is a reasonable technique for early malignancies of the gland when complete resection can be achieved and when there is no evidence of local invasion. However, we suggest conversion to open surgery in lesions when clear evidence of malignancy is discovered during the surgical procedure.

We adhere to what is stated in the international literature regarding laparoscopic adrenal metastasectomies; in our series, resection was technically feasible due to smaller, usually intraglandular tumours in 7 surgical cases, and results were better than those from alternative treatments.

Conflicts of interest

The authors affirm that they have no conflicts of interest.

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