Laparoscopic adrenalectomy: pathologic features determine outcome

Eric C. Poulin, MD; Christopher M. Schlachta, MD; Stephen E. Burpee, MD; Kenneth T. Pace, MD; Joseph Mamazza, MD

Introduction: The differential outcomes of laparoscopic adrenalectomy are not well described. Therefore, we evaluated these outcomes in the 3 groups most often seen clinically: bilateral adrenalectomy for Cushing's disease (group 1), pheochromocytoma (group 2) and unilateral adrenalectomy for non-pheochromocytoma (group 3). **Methods:** We reviewed a longitudinal database of 72 consecutive cases of laparoscopic adrenalectomy carried out between 1997 and 2001 at the Centre for Minimally Invasive Surgery, University of Toronto. **Results:** Patients in group 1 tended to be older (median 49 yr) and heavier (median 87 kg). They had a longer operating time (median 255 min), more postoperative complications (15%) and a longer median postoperative stay (4 d). Patients in group 2 had intermediate outcomes: a median operating time of 198 minutes, complication rate of 8.3% and a median postoperative hospital stay of 3 days. However, they had more intraoperative blood loss (median 150 mL). Group 3 patients had the best outcomes with the shortest median operating time (125 min), least blood loss (median 50 mL), fewer complications (6%) and shortest hospital stay (median 2 d). **Conclusions:** Although the outcomes of laparoscopic adrenalectomy are uniformly good, on the basis of the underlying pathologic characteristics, patients can be divided into groups that have different expected outcomes. Patients requiring a unilateral adrenalectomy except for pheochromocytoma have the best recorded outcomes. Surgeons transferring to laparoscopic adrenalectomy would benefit from selecting patients in this group during their learning curve.

Introduction : Les résultats différentiels de la surrénalectomie par laparoscopie ne sont pas bien décrits. C'est pourquoi nous avons évalué ces résultats dans les trois groupes les plus courants en contexte clinique : la surrénalectomie bilatérale contre la maladie de Cushing (groupe 1), le phéochromocytome (groupe 2) et la surrénalectomie unilatérale chez les patients non atteints de phéochromocytome (groupe 3). **Méthodes :** Nous avons passé en revue une base de données longitudinales sur 72 cas consécutifs de surrénalectomie par laparoscopie pratiquée entre 1997 et 2001 au Centre de chirurgie à effraction minimale de l'Université de Toronto. **Résultats :** Les patients du groupe 1 avaient tendance à être plus âgés (médiane, 49 ans) et plus lourds (médiane, 87 kg). Dans ce groupe, l'intervention était plus longue (médiane, 255 minutes), il y a eu un plus grand nombre de complications postopératoires (15 %) et l'hospitalisation postopératoire médiane était plus longue (4 jours). Les patients du groupe 2 ont présenté des résultats intermédiaires : une durée médiane d'intervention s'établissant à 198 minutes, un taux de complications de 8,3 % et une hospitalisation postopératoire médiane de 3 jours. En revanche, la perte de sang pendant l'intervention était plus importante dans ce groupe (médiane, 150 mL). Les patients du groupe 3 ont présenté les meilleurs résultats : l'intervention la plus courte (125 minutes), la moindre perte de sang (médiane, 50 mL), le moins de complications (6 %) et l'hospitalisation la plus courte (médiane, 2 jours). **Conclusions :** Encore que les résultats de la surrénalectomie par laparoscopie soient uniformément bons, en se fondant sur des caractéristiques pathologiques sous-jacentes, il est possible de répartir les patients en groupes qui s'accompagnent de différents résultats prévus. Les patients qui ont besoin de subir une surrénalectomie unilatérale pour une autre affection que le phéochromocytome présentent les meilleurs résultats observés. Les chirurgiens qui commencent à pratiquer la surrénalectomie par laparoscopie gagneraient à choisir des patients dans ce groupe tandis qu'ils suivent leur courbe d'apprentissage.

Correspondence to: *Dr. Eric C. Poulin, Chief of Surgery and Surgical Services, Box 175, Ottawa Hospital–General Campus, 501 Smyth Rd., Ottawa ON K1H 8L6; fax 613 739-6769; EPoulin@ottawahospital.on.ca*

Since the original work of Gagner and associates,[1,2] laparoscopic adrenalectomy has become the standard of care for benign adrenal disorders. Despite confirmation by many authors of favourable outcomes traditionally associated with minimally invasive procedures, we have observed that these outcomes vary with respect to adrenal disease. We therefore reviewed our experience with laparoscopic adrenal surgery to determine if outcomes of laparoscopic adrenalectomy differ from one clinical situation to another.

Patients and methods

All consecutive cases of laparoscopic adrenalectomy performed in the Centre for Minimally Invasive Surgery at St. Michael's Hospital, Toronto, a tertiary teaching centre, between December 1997 and December 2001 were included in a prospectively collected database and form the basis of this review. The data collected included demographic information, age, weight, diagnosis, endocrine investigation, comorbid conditions, history of previous surgery, procedure, operating time, intraoperative blood loss, size and location of extraction incision, transfusions, conversion to open surgery, record of intraoperative and postoperative complications and time of discharge from hospital. Operating time was defined as time elapsed between first incision and last skin suture. Information on long-term follow-up was obtained from hospital or office charts. If insufficient, this was supplemented by phone calls to referring physicians and patients.

All procedures were performed transperitoneally in the lateral position with 3 or 4 subcostal trocars (5 mm and 12 mm). For needlescopic procedures, two 3-mm trocars were used in the subcostal region and a 12-mm trocar at the umbilicus, along with 3-mm and 10-mm laparoscopes. For bilateral adrenalectomy, the left side was done first.

The patient was then turned and prepared for right adrenalectomy. Glands were placed in a sterile plastic bag and were extracted through enlargement of a subcostal trocar site, or from the umbilicus for needlescopic procedures. Specimens were not fragmented. However, for larger specimens, mainly pheochromocytomas or incidentalomas, specimens were cut in pieces within the plastic bag after agreement with the pathologist. Adrenal cysts were aspirated within the extraction bag before removal.

Clinical observation of operative procedures and postoperative evolution led us to identify 3 groups of patients who seem to respond differently, and they served as the basis for this analysis: 13 patients (group 1) who underwent bilateral adrenalectomy for Cushing's disease; 12 patients (group 2) with pheochromocytomas; and 33 patients (group 3) who underwent unilateral adrenalectomy for reasons other than pheochromocytoma.

Unless stated otherwise, all values are expressed as the median (and range). Statistical analysis consisted of the χ^2 test, 1-way analysis of variance (ANOVA), and the Kruskal–Wallis 1-way ANOVA on ranks. For pairwise comparisons, the Bonferoni t-test or Dunn's method were used where appropriate. A p value of 0.05 or less was considered statistically significant.

Results

Seventy-two laparoscopic adrenalectomies were performed on 58 patients. Bilateral adrenalectomies were done for 13 patients with Cushing's disease and 1 patient with bilateral pheochromocytoma. There were 23 men and 35 women, median (and range) age 46 (24–81) years and weight 71 (39–122) kg. The size of the excised lesions was 4.5 (0.9–18) cm in diameter.

The excised glands were larger than 6 cm in 16 patients (22%). Two adrenal cysts were respectively 10 and 18 cm in size. The larger glands were found in patients with pheochromocytoma (5), Cushing's hyperplasia (5), incidentalomas (3) and primary hyperaldosteronism (3). The size of the tumour did not change the outcome for the patients within their assigned group in regard to operating time, intraoperative complications, estimated blood loss, postoperative complications and length of stay, with 2 exceptions. One 79-year-old patient with pheochromocytoma and atrial fibrillation sustained an intraoperative tear of the vena cava repaired laparoscopically. His operating time was 300 minutes, estimated blood loss was 1000 mL and length of hospital stay was 12 days because of postoperative pneumonia and an attack of gout. Another pheochromocytoma patient with neurofibromatosis had inadequate preoperative pharmacologic blockade. His intraoperative blood pressure was very labile and his gland oozed continuously. His operating time was 260 minutes, and blood loss was 1000 mL. Nevertheless, he was discharged from hospital on the third postoperative day.

Comorbid conditions were present in 37 (64%) of the 58 patients; they were cardiovascular in nature in 34 of these. Hypertension was present in 25 patients. Values for the whole cohort were as follows: operating time, 150 (55–430) minutes; operative blood loss 75 (0–1000) mL and extraction incision 1.5 (1–6) cm. Blood loss was less than 100 mL in two-thirds of patients. Only 2 (3.4%) patients received intraoperative blood transfusion. Both were severely pancytopenic and had bilateral adrenalectomy for Cushing's disease. One of these patients also received transfusions postoperatively.

Intraoperatively, 7 patients (12%) had complications, and all but 1 of the complications were dealt with laparoscopically. An inferior vena caval tear (7-cm right pheochromocytoma), a left renal vein tear (Cushing's disease), a cautery burn to the

left diaphragm (left Cushing's adenoma), and a serosal tear to the colon (left 2-cm primary hyperaldosteronism) required laparoscopic suturing. A liver laceration (Cushing's disease) and continuous oozing from a left pheochromocytoma both required surgical packing laparoscopically. Finally, a vascular surgeon was called in to repair a carotid tear from insertion of a central venous line during induction in a patient with Conn's syndrome. There were no conversions to open surgery, but 1 procedure was not started after induction of anesthesia because the patient was very unstable, with systolic blood pressures measured above 280 mm Hg in a blocked pheochromocytoma. There were no postoperative deaths. For the entire cohort, the time to discharge from hospital was 2 (1–33) days. Discharge occurred on the first postoperative day in 10 patients (17%), on the second postoperative day in 22 patients (38%) and third postoperative day in 14 patients (24%). Of the remaining 12 patients, 4 stayed 10 days or longer because of postoperative complications and 8 stayed 4–6 days. The preoperative diagnosis in the 12 patients with hospital stays over 3 days were Cushing's disease (7), pheochromocytoma (3), hyperaldosteronism (1) and single nonsecreting adenoma (1).

Bilateral adrenalectomy for Cushing's disease (group 1)

The relatively large number (13) of patients in this group is related to the referral of these cases to an expert in pituitary surgery in our centre. All of these patients had failed 1 or more previous pituitary procedures or radiation to the pituitary gland. They all represented cases of end-stage Cushing's disease. Four patients with single adrenal cortisol-producing adenomas were assigned to group 3.

In this group, values for age and weight were 49 (24–78) years and 87 (51–122) kg. These hyperplastic glands that did not contain tumours were 5.7 (2–8.5) cm in size. All patients in this group had at least 1 comorbid condition. Operating time was 255 (115–430) minutes and blood loss was 100 (25–600) mL (Table 1). The size of the gland extraction site was 1.4 (1.2–2) cm. The only 2 transfused patients were in this group. The decision to transfuse was made not so much because of blood loss, but because of severe pancytopenia. Two (15%) of the 13 patients had postoperative complications. One had to be transferred to the intensive care unit for hypercapneic respiratory failure and steroid-induced delirium. The other patient had aspiration pneumonia, confusion and generalized weak-

ness. This patient with end-stage Cushing's disease was discharged after 33 days in hospital. She died of her disease a few months later. Hospital stay was 4 (2–33) days. None of the patients in this group was able to leave on the first postoperative day, only 1 left on day 2, and the 3 of the 4 longest stays were from this group (33, 16 and 10 d).

Pheochromocytoma (group 2)

Twelve patients were treated for pheochromocytoma, 1 had both adrenal glands excised for bilateral lesions. One patient with multiple endocrine neoplasia (MEN, type 2) syndrome had a previous thyroidectomy for medullary carcinoma and another had von Recklinhausen's neurofibromatosis. One pregnant woman was operated on at 14 weeks' gestation. Their age and weight were, respectively, 45 (24–81) years and 68 (46–113) kg. The distribution of lesions was equal between the left and right side. The size of pheochromocytomas ranged from 2.6–8 cm (median 4.5 cm). Operating time was 197 (130–300) minutes, intraoperative blood loss 150 (25–1000) mL and size of the extraction incision 3 (1.5–6) cm. No patient was transfused. Only 1 patient, a 78-year-old man, had postoperative complications (8%). He had pneumonia and a gout

Table 1

Laparoscopic Adrenalectomy Outcomes

Characteristics	Group 1, n = 13	Group 2, n = 12	Group 3, n = 33	p value	p < 0.05
Age, yr (mean (and SD))	50.8 (15.5)	52.1 (18.6)	45.7 (12.3)	NS	
Weight, kg (mean (and SD))	85.2 (22.0)	70.4 (18.1)	67.7 (17.1)	0.027	Group 3 v. group 1*
Operating time, min† (median (and range))	255 (115–430)	197 (130–300)	125 (55–310)	< 0.001‡	Group 1 v. group 3 and group 2 v. group 3§
Estimated blood loss, mL (median (and range))	100 (25–600)	150 (25–1000)	50 (0–300)	0.006‡	Group 1 v. group 3 and group 2 v. group 3§
Complications, % Intraoperative	23	16	3		
Postoperative	15	8	6	NS	
Length of hospital stay, d (median (and range))	4 (3–33)	3 (2–12)	2 (1–5)	< 0.001	Group 1 v. group 3 and group 2 v. group 3§

SD = standard deviation; group 1 = bilateral adrenalectomy for Cushing's disease; group 2 = pheochromocytoma; group 3 = unilateral adrenalectomy for non-pheochromocytoma.
*Bonferoni t-test
†Defined as time elapsed from first incision to last skin suture.
‡Kruskal–Wallis 1-way analysis of variance
§Dunn's method

attack. The hospital stay was 3 (2–12) days. None of the pheochromocytoma patients left after an overnight stay. However, 42% left on the second postoperative day and 75% had left hospital by day 3. This is largely related to the time required to ensure stability of blood pressure, cardiac rhythm and fluid balance.

Unilateral adrenalectomy for reasons other than pheochromocytoma (group 3)

The diagnoses for the 33 patients who had unilateral adrenalectomy for reasons other than pheochromocytoma are described in Table 2. In this group, values for age and weight were 44 (26–68) years and 65 (39–112) kg respectively. Lesion size was 3 (0.9–18 cm) cm. The ratio of left adrenalectomy to right adrenalectomy was 21:12. Needlescopic surgery was only attempted in this group (5 patients). One was transformed to standard laparoscopic technique. Extraction incision size was 1.5 (1–3.4) cm. Operating time was 125 (55–310) minutes and blood loss was 50 (range from 0–300) mL. Patients in this group had a significantly shorter operating time than patients in groups 1 and 2 ($p < 0.001$) There was also a significantly lower blood loss between patients in group 3 and in groups 1 and 2 ($p < 0.006$). A 2-day ileus and hypotension on the first postoperative day were the only complications recorded (6%). The hospital stay was 2 (1–5) days, being

Table 2

Diagnoses for Unilateral Adrenalectomy, Excluding Pheochromocytoma (Group 3)

Diagnosis	No. of patients
Conn's syndrome	21
Nonfunctioning cortical adenomas (> 5 cm)	5
Cushing's adenoma	4
Adrenal cyst	2
Paraganglioma	1
Total	33

significantly shorter than in groups 1 and 2 ($p < 0.001$) (Table 1). In regard to hospital stay, 30% of patients left after an overnight stay and 79% had gone home by the second postoperative day. Only 1 patient went home after 3 days in hospital.

Outcomes for right versus left adrenalectomy

When the outcomes for patients having a right versus a left adrenalectomy, including patients with pheochromocytomas, were analyzed to determine if there were different outcomes based on differences in adrenal anatomy on each side, no difference was found. There was no difference in age (45 v. 44 yr), weight (64 v. 68 kg), extraction incision size (1.75 cm for both), operating time (135 min for both), blood loss (50 mL for both) and hospital stay (2 d for both).

Discussion

Laparoscopic adrenalectomy is now accepted as the standard of care for most adrenal disorders despite the absence of randomized clinical trials to validate its adoption. However, there exist many nonrandomized, case-matched comparative studies and clinical series from all over the world describing superior, patient-friendly outcomes.[3–14] The quality of observed outcomes, once the learning curve is past, makes it very unlikely that randomized trials testing the laparoscopic approach versus the open approaches will ever be done.

However, the patient profile for this procedure is far from being monolithic, and patients from the 3 groups defined earlier have singular issues that may help define differences in their expected outcomes.

Bilateral adrenalectomy for Cushing's disease (group 1)

The patients who have pituitary-dependent Cushing's disease repre-

sent roughly 90% of patients with this condition. When they are referred for bilateral adrenalectomy, it is usually for failure of previous treatments. They have had 1 or more attempts at excision of a pituitary adenoma followed by recurring symptoms and documented recurrence. Occasionally, for malignant disease, radiotherapy is used. This process takes many months and is reflected in the general condition of the patient. Most of the stigmata of the disease are present. Patients are hypertensive, have parchment-like skin, feel weak, do not tolerate sepsis well, bruise easily, have poor overall tissue quality and are obese. This makes surgery more difficult.

These characteristics are well represented in this series in which 13 such patients were treated by laparoscopic bilateral adrenalectomy. Patients from this group tended to be older and heavier. Although the differences were not statistically significant for the 3 groups, there is a significant difference for weight between patients in groups 1 and 3 ($p = 0.027$). They had a longer operation because of the bilateral nature of the procedure, and their hospital stay was the longest, being twice as long as patients in group 3. Postoperative complications (15%) were more than twice as frequent as in group 3 (6%) and almost twice as frequent as patients with pheochromocytoma (8%), although the differences were not significant ($p = 0.675$) (Table 1). These outcomes can be explained by the multiple factors of increased age and weight, a longer procedure, a poorer general condition and the bilaterality of the surgery.

Pheochromocytoma (group 2)

The morbidity of pheochromocytoma patients is largely related to the hypersecretion of adrenergic and noradrenergic hormones, the preoperative blockade and the postexcision fluid shifts.

Unilateral adrenalectomy for pheochromocytoma takes about 1 hour longer than unilateral adrenalectomy for other causes (group 3). This procedure, by design, is meticulous and deliberate. Strategically, the procedure is paused when there is a rise in blood pressure to avoid large swings that could endanger the patient. The fact that pheochromocytomas are on average twice the size of hyperaldosteronomas also plays a role. Furthermore, great care must be exerted to avoid capsular breaches and the possibility of iatrogenic pheochromocytomatosis.[15] The same care should also apply to adrenalectomy for Cushing's disease as cortical cells can be implanted by careless technique and cause recurrent disease. Despite all that attention, unilateral adrenalectomy for pheochromoytoma yielded the highest blood loss of the 3 groups (150 mL v. 100 mL and 50 mL).

Postoperative complications occurred in 8% of patients in this group, between the complications rates for groups 1 (15%) and 3 (6%). Similarly, the hospital stay was 3 days versus 4 and 2 days, respectively, for groups 1 and 3.

Unilateral adrenalectomy for reasons other than pheochromocytoma (group 3)

Group 3 comprises patients with various diagnoses, except pheochromocytoma, who require a unilateral adrenalectomy (Table 2). Primary hyperaldosteronism and cortisol-secreting adenomas represent the only functional tumours in this group. These tumours are usually small and easy to manage intraoperatively. Also, the patients tend to be in better physical shape than patients in the other 2 groups, and no complicated preoperative preparation is required.

The 33 patients in this group had the shortest operations (125 min) with the least blood loss (50 mL) and the shortest hospital stay (2 d). The team caring for these patients envisions the distinct possibility of caring for many in this group as outpatients within a 23-hour recovery room environment when this becomes available.[16,17] Patients from group 3 represent the best outcomes in laparoscopic adrenal surgery. They are also the easiest to care for with simple perioperative care.

Conclusions

Although outcomes of laparoscopic adrenalectomy are uniformly good, patients can be classified into groups with different expected outcomes, largely due to their underlying disease features. Patients requiring a unilateral adrenalectomy except for pheochromocytoma have the best recorded outcomes. Surgeons transferring to laparoscopic adrenalectomy would benefit from selecting patients in that group during their learning curve. Capsular breaches during surgery should be avoided to prevent recurrent disease in patients operated on for pheochromocytoma and Cushing's disease.

References

1. Gagner M, Lacroix A, Bolte E. Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma [letter]. *N Engl J Med* 1992;327:1033.
2. Gagner M, Lacroix A, Bolte E, Pomp A. Laparoscopic adrenalectomy. The importance of a flank approach in the lateral decubitus position. *Surg Endosc* 1994;8:135-8.
3. Dudley NE, Harrison BJ. Comparison of open posterior versus transperitoneal laparoscopic adrenalectomy. *Br J Surg* 1999;86:656-60.
4. Toniato A, Bernante P, Rosse GP, Piotto A, Pelizzo MR. Laparoscopic versus open adrenalectomy: outcome in 35 consecutive patients. *Int J Surg Investig* 2000;1:503-7.
5. Hazzan D, Shiloni E, Golijanin D, Jurim O, Gross D, Reissman P. Laparoscopic vs open adrenalectomy for benign adrenal neoplasm. *Surg Endosc* 2001;15:1356-8.
6. Edwin B, Kazaryan AM, Mala T, Pfeffer PF, Tonnessen TI, Fosse E. Laparoscopic and open surgery for pheochromocytoma. *BMC Surg* 2001;1:2.
7. Schell SR, Talamini MA, Udelsman R. Laparoscopic adrenalectomy for nonmalignant disease: improved safety, morbidity, and cost-effectiveness. *Surg Endosc* 1999;13:30-4.
8. Imai T, Kikumori T, Ohiwa M, Mase T, Funahashi H. A case-controlled study of laparoscopic compared with open lateral adrenalectomy. *Am J Surg* 1999;178:50-4.
9. Winfield HN, Hamilton BD, Bravo EL, Novick AC. Laparoscopic adrenalectomy: the preferred choice? A comparison to open adrenalectomy. *J Urol* 1998;160:325-9.
10. Brunt LM, Doherty GM, Norton JA, Soper NJ, Quasebarth MA, Moley JF. Laparoscopic adrenalectomy compared to open adrenalectomy for benign adrenal neoplasms. *J Am Coll Surg* 1996;183:1-10.
11. Gagner M, Pomp A, Heniford BT, Pharand D, Lacroix A. Laparoscopic adrenalectomy: lessons learned from 100 consecutive procedures. *Ann Surg* 1997;226:238-7.
12. Guazzoni G, Cestari A, Montorsi F, Lanzi R, Nava L, Centemero A, et al. Eight-year experience with transperitoneal laparoscopic adrenal surgery. *J Urol* 2001;166:820-4.
13. Lezoche E, Guerrieri M, Paganini AM, Feliciotti F, Zenobi P, Antognini F, et al. Laparoscopic adrenalectomy by the anterior transperitoneal approach: results of 108 operations in unselected cases. *Surg Endosc* 2000;14:920-5.
14. Gill IS. The case for laparoscopic adrenalectomy. *J Urol* 2001;166:429-36.
15. Li ML, Fitzgerald PA. Iatrogenic pheochromocytomatosis: a previously unreported result of laparoscopic adrenalectomy. *Surgery* 2001;130:1072-7.
16. Rayan SS, Hodin RA. Short-stay laparoscopic adrenalectomy. *Surg Endosc* 2000;14:568-72.
17. Gill IS, Hobart MG, Schweizer D, Bravo EL. Outpatient adrenalectomy. *J Urol* 2000;163:717-20.