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Surgical Management of Adrenal Disorders: The Triumph of Minimally-invasive Surgery

BY KENNETH PACE, MD, MSc, FRCSC

There has been a revolution in surgical practice over the last decade that has seen minimally-invasive surgical techniques applied to a broad range of operative procedures. Adrenalectomy is one example of the dramatic benefits that laparoscopic surgery can offer patients, while replicating the benefits of open surgery. This issue of *Endocrinology Rounds* reviews the history, indications, contraindications, technique, and outcomes of laparoscopic adrenalectomy.

Background

The adrenal gland was first described in 1552 by Bartholomaeus Eustachius, somewhat poetically as "*glandulare renis incumbens*" or "the gland that sleeps with the kidney." It took more than three centuries, however, before the first reported adrenalectomy was successfully performed by Knowsley-Thorton in London and it was not until the 1930s that adrenalectomy became popularized via the posterior approach described by Hugh Hampton Young. Nevertheless, the relative inaccessibility of the adrenal glands high in the retroperitoneum meant that, for much of the twentieth century, open adrenal surgery was a daunting proposition. Long, muscle-dividing, subcostal or flank incisions were required to access the adrenal glands safely. This meant that patients faced a long post-operative hospital stay and recovery period, as well as significant risks for wound-related, pulmonary, and cardiac complications.

By the end of the 20th century, surgical pioneers were again pushing the envelope and applying the minimally-invasive surgical techniques used for cholecystectomy to more advanced surgical procedures. In 1992, Michel Gagner extended this revolution to adrenal surgery when he performed the first laparoscopic adrenalectomy for a cortisol-producing adenoma.¹ Since that time, refinements in equipment and technique have expanded the role of laparoscopy in surgical adrenal disease so that it is now the standard of care for most adrenal pathologies.

Laparoscopic adrenalectomy

Laparoscopy, or minimally-invasive surgery (MIS), represents a paradigm shift in the surgical approach. The goal of laparoscopy is to replicate open surgical principles, while minimizing surgical trauma, providing the patient with a shorter surgical recovery time. This is accomplished using carbon dioxide insufflation of the peritoneal cavity at a pressure of 15 mm Hg to provide a working space, followed by the use of 3 to 4 small incisions (3 to 12 mm each) to allow insertion of a camera and specialized instruments to perform the procedure (Figure 1). Using MIS techniques, laparoscopic adrenalectomy can be carried out with incisions that are 1 cm or less, rather than a 20 to 30 cm long flank or subcostal incision. Resultant dramatic patient benefits include a shorter hospital stay, less post-operative pain, less blood loss, fewer wound-related complications, superior visualization during the operation because of



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Figure 1: Operative photo of laparoscopic left adrenalectomy



optical magnification, and fewer pulmonary complications (eg, pneumonia and atelectasis) because patients have less post-operative impairment in forced expiratory volume (FEV₁) and vital capacity.

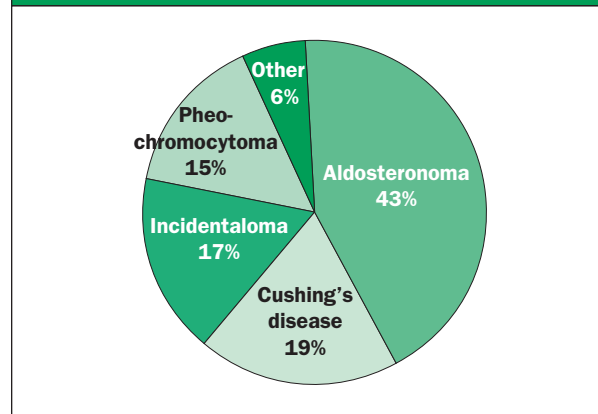
Indications

Initially, laparoscopic adrenalectomy was reserved for small adrenal tumours in carefully selected patients but, with advances in surgical instrumentation and technique, MIS approaches can now be used safely and effectively for the vast majority of adrenal pathologies. The indications for laparoscopic adrenalectomy are virtually identical to those for open surgery and include functional adrenal tumours; selected cases of bilateral adrenal hyperplasia; patients with Cushing's disease refractory to other therapies; non-functional adrenal tumours >4 cm or those that demonstrate growth on serial imaging or have radiologic features suggestive of malignancy; and selected cases of solitary adrenal metastases (Figure 2). Contraindications to laparoscopy are also very similar to those for open surgery: uncontrolled bleeding diathesis and poor blood pressure control in pheochromocytoma patients.

Aldosteronoma

Aldosterone-producing adrenal adenomas are the indication for surgery in 40% to 50% of patients undergoing adrenalectomy. The diagnosis is generally suspected in a hypertensive patient with hypokalemia in the absence of diuretics and is then confirmed when there is a high plasma aldosterone level and high plasma aldosterone-to-plasma renin activity. The diagnosis can also be confirmed with a 24-hour urine collection for aldosterone following an oral salt load

Figure 2: Indications for adrenalectomy⁷



or with selective adrenal venous sampling. Treatment consists of lifelong antihypertensive agents, often with a potassium-sparing diuretic and potassium supplementation, or adrenalectomy. Prior to the laparoscopic era, many patients were unwilling to undergo the risks and morbidity of open surgery and the majority favoured medical therapy. Today, however, laparoscopic adrenalectomy offers patients a surgical cure for hyperaldosteronism and a more rapid recovery. Multiple series have demonstrated that adrenalectomy cures hyperaldosteronism in virtually 100% of patients and eliminates the need for potassium supplementation. The vast majority of patients also have either improvement or normalization of blood pressure post-operatively.² Older patients, patients with long-standing hypertension, and those who require multiple antihypertensive agents pre-operatively may have co-existing arteriosclerosis or essential hypertension, and so may still require antihypertensive therapy post-operatively, but generally with fewer agents than pre-operatively.

Cushing's Syndrome

Patients with cortisol-producing adrenal adenomas generally present with high 24-hour urine free cortisol and suppressed adrenocorticotrophic hormone (ACTH) levels. These patients also benefit greatly from laparoscopic adrenalectomy. High pre-operative cortisol levels increase the risks for wound-related complications (eg, infection and herniation), risks that are dramatically lower with laparoscopy than with open surgery. Furthermore, laparoscopy is associated with fewer post-operative pulmonary effects. In particular, there is less impact on FEV₁ and forced vital capacity (FVC), with a lower risk of post-operative atelectasis and pneumonia; these are important considerations in these often debilitated patients. Patients

with pituitary adenomas and Cushing's disease that is refractory to other interventions (eg, trans-sphenoidal surgery) can also benefit from laparoscopic bilateral adrenalectomy.

Pheochromocytoma

These catecholamine-secreting tumours can be difficult to both diagnose and manage. Plasma metanephrine levels are likely the most sensitive and specific laboratory investigation. Magnetic resonance imaging (MRI) and metaiodobenzylguanidine (MIBG) scanning can also be a useful adjunct to computed tomography (CT) scanning in localizing a pheochromocytoma, particularly extra-adrenal and bilateral disease. The vast majority of adrenal pheochromocytomas are amenable to laparoscopic procedures.³ A multidisciplinary approach is important for optimizing the preparation of these patients for the operating room, with collaboration between the endocrinology, anesthesia, and urology departments. Pre-operative preparation with non-competitive alpha-blockers (eg, phenoxybenzamine), in conjunction with salt- and fluid-loading, can help minimize dramatic intra-operative swings in blood pressure.

Initially, it was felt that the pneumoperitoneum used for laparoscopy increased catecholamine secretion from these tumours, leading to greater difficulties in intra-operative blood pressure control compared to open surgery, but this is not the case. A number of investigators have shown that with appropriate surgical technique, including minimal handling of the adrenal gland intra-operatively and early ligation of the adrenal vein, laparoscopic adrenalectomy is safe and less morbid than open surgery.^{4,5} Occasionally, a large (>10 cm) or very active pheochromocytoma can be difficult to manage laparoscopically and may require open surgery, but these are a distinct minority. These lesions are best managed in centres where invasive intra- and post-operative hemodynamic monitoring is available to allow for rapid correction of blood pressure swings and arrhythmias. They often require post-operative monitoring in an intensive care unit environment, with longer post-operative stays than other adrenal pathologies.⁶

Incidentaloma

Increased use of cross-sectional imaging has led to a dramatic increase in the diagnosis of asymptomatic adrenal lesions, with a prevalence of 0.6% to 4.4% of abdominal CT scans⁷ and 8.7% to 14% of autopsy series.⁸ In addition, these lesions become more common with increasing patient age (3% to 7% inci-

dence for patients aged >50 years compared with <1% for those <30 years). Overall, approximately 15% are hormonally active,⁹ but the risk of endocrine activity is directly proportional to lesion size, with 40% of lesions >6 cm having some function.¹⁰ A National Institutes of Health (NIH) consensus conference¹¹ recommends that patients with an adrenal incidentaloma be evaluated with a serum potassium, a low-dose dexamethasone suppression test, or a 24-hour urine free cortisol and, if hypertensive, urinary catecholamines and metanephrines and a plasma aldosterone-to-plasma renin activity ratio. Nonfunctional lesions <4 cm can be observed with serial imaging, while those \geq 6 cm should be excised as the risk of occult adrenocortical carcinoma rises with lesion size. CT scanning can often help narrow the differential between adenoma and carcinoma, as adrenal adenomas are classically lipid-rich, with CT densitometry of 1 to 10 Hounsfield units on non-contrast scanning, while adrenal cancers are more heterogeneous, with higher CT density of >20 Hounsfield units.¹² "Chemical shift" techniques with MRI are occasionally helpful for cases that are indeterminate on CT and have densities of between 10 and 20 Hounsfield units.¹²

Adrenocortical carcinoma

Adrenal cancer is a rare and dreaded problem, as patients often present with advanced disease that can be refractory to both medical and surgical therapy. Imaging often suggests the diagnosis with large, heterogeneous, poorly-demarcated adrenal masses associated with venous invasion, regional adenopathy, or metastases. Adrenal cancers can be encountered unexpectedly in otherwise benign-appearing, but large adrenal lesions. Laparoscopy can be offered to many patients with smaller (<10 cm) adrenal cancers, without compromise of cancer control.¹³ Large, locally-advanced adrenal carcinomas are still best managed with open surgery as they often require extensive resections to maximize the chance of cure.

Non-endocrine adrenal lesions

The differential diagnosis of adrenal lesions is broad and encompasses a variety of nonendocrine causes, including metastases to the adrenal, myelolipoma, cysts, infectious processes such as tuberculosis and fungi, adrenal hemorrhages, lymphoma, and amyloidosis. These other diagnoses need to be considered before proceeding with adrenalectomy for lesions that are not hormonally active. Percutaneous biopsy can occasionally be useful for suspected metastatic lesions, but should only be carried out after a

thorough evaluation to rule-out pheochromocytoma. Laparoscopic adrenalectomy may be indicated for isolated metastases to the adrenal and can provide durable disease-free survival in carefully-selected patients,¹⁴ particularly those with renal cell carcinoma and pulmonary small cell carcinoma primaries.

Techniques

There are a variety of techniques for performing an MIS adrenalectomy. The most common approach is the transperitoneal laparoscopic approach, but extraperitoneal (or retroperitoneoscopic) approaches also exist. There are no significant differences in length of stay, blood loss, or patient recovery between these two MIS techniques.^{15,16}

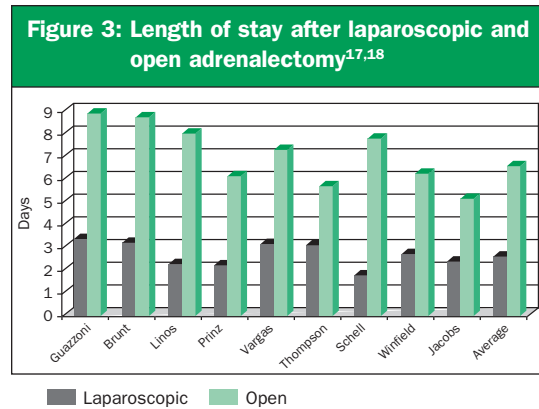
Laparoscopic adrenalectomy can be performed via 3 trocar incisions on the left side and 4 on the right (the fourth trocar is required to retract the liver). Right- and left-sided procedures are quite different since adrenal anatomy is different from one side to the other.

On the left side, the spleen, the tail of the pancreas, and splenic flexure of the colon must be mobilized in the transperitoneal approach to expose the adrenal gland and the adrenal vein that drains into the left renal vein. On the right side, the liver must be mobilized to expose the inferior vena cava into which the adrenal vein drains. Regardless of the approach, adrenalectomy can generally be carried out as a short-stay procedure and patients are generally discharged home within 24 hours of surgery. In cases where cosmesis is particularly important, the camera trocar can be placed in the umbilicus and 2 or 3 mm “needlescopic” ports can be used to perform the procedure; the adrenal can then be removed through the umbilical incision. Post-operatively, the umbilical incision is not visible and the “needlescopic” scars are little larger than the scars left from 14 gauge angiocatheters.

Outcomes

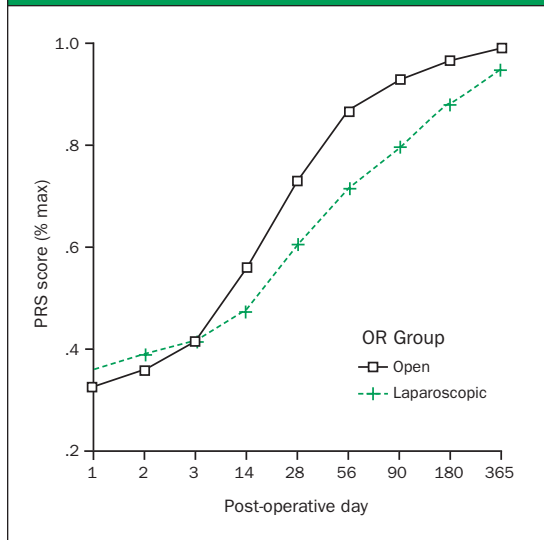
Adrenal surgery is possibly the most dramatic example of the benefits of laparoscopy over open surgery. The small size of the adrenal gland (and thus the small size of the extraction incision) and its relative inaccessibility for open surgery make it the ideal subject for laparoscopy. The benefits include:

- Hospital length of stay is dramatically shorter for laparoscopy (1.7 versus 7 days for a series of 9 surgical series, $p < 0.001$).



- Operative times are quite similar (160 versus 130 minutes, non-significant [NS]).
- Blood loss is significantly lower with laparoscopy (153 versus 355 cc, $p < 0.001$).
- Complication rates are dramatically lower (7% versus 24%, $p < 0.001$). This is particularly true for wound-related complications (infection and hernia) and pulmonary complications (pneumonia) that are both quite rare with laparoscopy and relatively common with open surgery.
- Post-operative narcotic usage is lower in laparoscopic adrenalectomy; patients require only 10% to 50% of the dose of narcotics used in open surgery patients, and have lower visual analog pain scores.
- Laparoscopy is also cost-effective; hospital costs are lower primarily because of the decreased length of stay (Figure 3) and total societal costs are lower because patients require less time to recover from surgery and return to work sooner.^{17,18}
- Perhaps the most important advantage is with health-related quality of life (HRQL). We examined the outcomes of 96 patients: 52 who had laparoscopic and 44 who had open surgery. HRQL was measured prospectively in all patients using a validated, modified version of the SF-36 instrument given at regular intervals post-operatively. HRQL returned to normal values much more rapidly following laparoscopic surgery and there was a persistent difference in HRQL, favouring laparoscopy even one year post-operatively (Figure 4).¹⁹ The explanation for these dramatic differences stems from the fact that flank and upper abdominal incisions divide large muscles and are quite painful in the post-operative period, particularly with respiratory movements and any bending or twisting maneuvers. In addition, approximately 10% of patients develop chronic wound issues such as hernias, bulges, or

Figure 4: Post-operative health-related quality of life (HRQL) after laparoscopic and open surgery¹⁹



Note: Y-axis indicates percent of pre-operative HRQL score; higher scores indicate higher HRQL. HRQL is higher for laparoscopy, $p < 0.001$.

nerve entrapment leading to chronic pain. These issues can essentially be completely avoided with laparoscopic approaches.

Limitations of laparoscopy

Conversion to open surgery can be a consequence of any laparoscopic procedure. However, in experienced hands, conversion rates for laparoscopic adrenalectomy are $< 5\%$ and are generally related to the underlying diagnosis. Large pheochromocytomas may be quite hormonally active, making blood pressure control during abdominal insufflation difficult. Very large tumours (> 10 to 12 cm) can be difficult to mobilize or may represent locally-invasive adrenal cancers, and may require open surgery. For the vast majority of surgical adrenal pathology, however, laparoscopy is safe and feasible.

Conclusions

Laparoscopic adrenalectomy provides numerous advantages for patients over open surgery, including less pain, fewer complications, less blood loss, shorter hospital stays, faster recovery times, and improved HRQL. It has now become the standard of care for the vast majority of benign adrenal pathologies, including more complex lesions such as pheochromocytoma. In fact, laparoscopic adrenalectomy has become so

attractive that many patients with primary hyperaldosteronism, who were previously reluctant to undergo open adrenalectomy because of the 7-day hospital stay and ≥ 3 -month recovery time, can now have the procedure performed on an outpatient basis and be back at work in 2 weeks. In the 21st century, open surgery has a very limited role for adrenal pathology and is essentially limited to very large tumours and adrenal cancers. The last decade has seen a triumph of laparoscopic adrenalectomy over open surgery, with dramatic benefits in post-operative quality of life.

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Abstracts of Interest

Laparoscopic versus open posterior adrenalectomy: a case-control study of 100 patients.

THOMPSON GB, GRANT CS, VAN HEERDEN JA, ET AL.
ROCHESTER, MN

BACKGROUND: Few controlled studies have compared laparoscopic transabdominal adrenalectomy (LA) to conventional open posterior adrenalectomy (PA).

METHODS: Five patients have undergone successful LA at our institution between 1992 and 1996. A matched case-control study of 50 PA patients was performed during a similar time period.

RESULTS: Follow-up was complete in 82% of patients with a mean follow-up time of 25 months. There were no statistically significant differences between the LA and PA groups with regard to the following demographic features: age, gender, endocrine disorder, side and size of tumor, and body habitus. Statistically significant differences ($p < 0.05$), however, were present (LA vs PA) when we compared the following results: mean hospital stay (3.1 versus 5.7 days), narcotic equivalents (28 versus 48), return to normal activity (3.8 versus 7 weeks), patient satisfaction (9 versus 7 [scale 1 to 10, 10 being most satisfied]), late morbidity (0 versus 54%), and operating room time (167 versus 127 minutes). Median hospital charges (\$7,000 versus \$6,000) were slightly higher in the LA group ($p = 0.05$).

CONCLUSIONS: Although LA is technically more demanding and slightly more expensive to perform, advances appear to exist for LA with regard to patient comfort, patient satisfaction, hospital stay, and return to normal daily activities. Late incisional complications are dramatically less in the LA group.

Surgery 1997;122(6):1132-6.

Surgical options in adrenalectomy: laparoscopic versus open surgery.

JANETSCHKE G. INNSBRUCK, AUSTRIA

Small hormone-active benign tumors are considered as clear indication for laparoscopic adrenalectomy. Laparoscopy resection of pheochromocytomas is still a controversial issue, but recent data have shown that the specific risks of pheochromocytoma surgery are not increased by the laparoscopic approach. The majority of endoscopic adrenalectomies are performed via the transperitoneal route, but there is growing interest in the retroperitoneoscopic approach. The advantages and disadvantages of each endoscopic approach have to be weighed carefully, but the final decision will also depend on the experience of the surgeon. Several retrospective studies have compared laparos-

copy with open surgery. There is general agreement that laparoscopy is superior to open surgery since it is associated with less pain, a shorter hospital stay, and more rapid return to normal activities, and also yields the best cosmetic and long-term results. Partial adrenalectomy may be indicated for bilateral pheochromocytoma, and also has advantages for patients with aldosterone-producing adenomas. The feasibility of laparoscopic partial adrenalectomy has been demonstrated. Laparoscopic intraoperative ultrasonography is valuable in selected cases. The already low morbidity of laparoscopic adrenalectomy can be reduced further by using needlescopic techniques.

Curr Opin Urol 1999;(3):213-8. Review

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