Original article

Retroperitoneal endoscopic adrenalectomy is safe and effective

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Background: The aim of this study was to review an experience with retroperitoneal endoscopic adrenalectomy (REA). This is the procedure of choice for adrenal tumours at this institution.

Methods: Between 1997 and 2008, 112 REAs were performed in a single university centre. Data were retrieved retrospectively from a prospectively collected database, including information on patient demographics, surgical procedure, complications and hospital stay.

Results: One hundred and twelve REAs were carried out successfully in 105 patients, including seven bilateral adrenalectomies. Thirty-nine patients with unilateral adrenal disease had a phaeochromocytoma, of whom 16 had multiple endocrine neoplasia syndrome type 2, 21 patients had Cushing's disease and 20 had Conn's disease. Median body mass index was 27 (interquartile range 23–29) kg/m^2. The median duration of unilateral operations was 100 (90–130) min with a median blood loss of 5 ml. Median tumour size was 3·1 (2·0–4·4) cm. Conversion from REA to open surgery was needed in two patients. Seven patients experienced postoperative complications (2 major, 5 minor). One patient needed a reoperation. The median postoperative hospital stay was 3 days. A learning curve with a significant decrease in operating time was observed over the years.

Conclusion: REA appears to be a safe and effective surgical technique for adrenal gland tumours up to 6 cm in diameter, with a minimal complication rate.

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Introduction

Laparoscopic adrenalectomy was first described in 1992 by Gagner and colleagues[1,2] and its advantages over open adrenalectomy soon became apparent in terms of less blood loss, fewer complications, less postoperative pain and a shorter hospital stay[3–6]. Hence laparoscopic adrenalectomy has become the standard treatment for adrenal gland tumours smaller than 6 cm[3,7–9]. Relative contraindications for the laparoscopic technique include larger tumours, signs of local invasion and primary adrenal malignancies.

The most frequently used endoscopic approach for adrenalectomy is the lateral transabdominal route[8,10–14]. The advantages of this technique are good exposure and availability of anatomical landmarks. Disadvantages are the higher chance of injury to intraperitoneal organs, abdominal adhesions and a longer operating time. Several other approaches have been reported, including the anterior transabdominal, lateral retroperitoneal and posterior retroperitoneal approaches. Because of the limited incidence of adrenal gland neoplasms, the number of comparative studies of the different approaches is limited, and the few available reports have shown minimal differences[4,15–17].

As the adrenal glands are located posteriorly in the retroperitoneum, it would appear logical to approach them directly from behind through the retroperitoneal 'space'. This approach was first reported by Walz and co-workers[18,19]. Potential advantages of this method are the direct route to the adrenals and a low chance of injury to abdominal organs. An additional advantage is the possibility of performing a bilateral excision without repositioning the patient[18,20,21]. Because of the limited working area with this approach, the technique seems more difficult and building experience takes time[22].

The aim of this study was to evaluate an experience with retroperitoneal endoscopic adrenalectomy (REA) in the second largest single-institution series worldwide.

Methods

Between October 1997 and December 2008, 105 patients underwent REA at the University Medical Centre Utrecht. Indications for REA were functional tumours, non-functional tumours generally smaller than 6 cm without signs of local invasion on preoperative imaging, and solitary metastases to the adrenals. Functional tumours included phaeochromocytomas and adrenal adenomas causing Cushing's disease, Conn's disease or testosterone overproduction. All non-functional tumours larger than 4 cm were considered eligible for surgery.

Data on patient characteristics, surgical procedure and outcome were retrieved from a prospectively assembled research database. All procedures were carried out by, or under the supervision of, one surgeon. The duration of operation was measured from skin incision to application of wound dressings.

Diagnosis

The preoperative diagnosis was based on a complete medical history, physical examination, laboratory tests and imaging studies. Hypercortisolism was established with a 1-mg dexamethasone suppression test and by measuring the 24-h urinary cortisone level. The plasma adrenocorticotrophic hormone (ACTH) level was measured to differentiate between ATCH-dependent and -independent Cushing's disease. Primary hyperaldosteronism was characterized by hypertension, hypokalaemia, increased plasma aldosterone and decreased plasma renin levels. Increased catecholamine levels in plasma and catecholamine metabolites (metanephrines) in urine collected over 24 h confirmed the diagnosis of phaeochromocytoma. A complete hormone analysis was performed in the event of an incidentaloma. Computed tomography and/or magnetic resonance imaging were used to localize adrenal tumours and measure their size. None of the patients who had Conn's disease underwent selective venous sampling.

Preoperative treatment

All patients with a phaeochromocytoma were treated with preoperative α- and β-blockers. All these patients were operated on under stringent monitoring (central venous line and arterial line). In patients with Conn's disease, electrolyte disturbances were corrected and blood pressure was regulated with spironolactone combined with extra medication if necessary. Patients with Cushing's disease were treated with a perioperative hydrocortisone stress schema. No prophylactic antibiotics were administered.

Operative technique

REA was performed under general anaesthesia. A technique slightly modified from that previously described by Walz and colleagues[19] was used. The patient was positioned in the prone position with the hips maximally flexed in order to create sufficient distance between the 12th rib and the iliac crest. The 12th rib along with the back muscles and iliac crest were marked with surgical ink followed by the trocar incision. For bilateral procedures, the sites were symmetrical (*Fig. 1*). A 2-cm transverse incision was made below the tip of the 12th rib. Next, subcutaneous tissue and muscles were separated. This was followed by digitally creating a space posterior from the kidney guided by its lower pole. The retroperitoneal space was increased by balloon dilatation. Two additional trocars were placed several centimetres cranial to the iliac crest with maximal lateral space between them. A blunt-tipped trocar was placed in the first incision and the retroperitoneal space was insufflated with carbon dioxide. The retroperitoneal space was insufflated to a pressure of 15 mmHg. In (morbidly) obese patients the maximum pressure used was 20 mmHg.

A 0° endoscope was used routinely. Guided by the diaphragm, the peritoneal sac was moved aside. The adrenal gland could easily be identified by its dark yellow colour and consistency (*Fig. 2*). Occasionally, a fourth trocar was placed to obtain more exposure but this was rarely necessary. The adrenal gland was dissected from its surroundings, both bluntly and with a LigaSure™ (Covidien, Dublin, Ireland) from the upper/lateral border to the plane with the kidney and finally to the hilum. The adrenal vein was clipped and divided. The entire adrenal gland was removed using an Endo Catch® retrieval bag

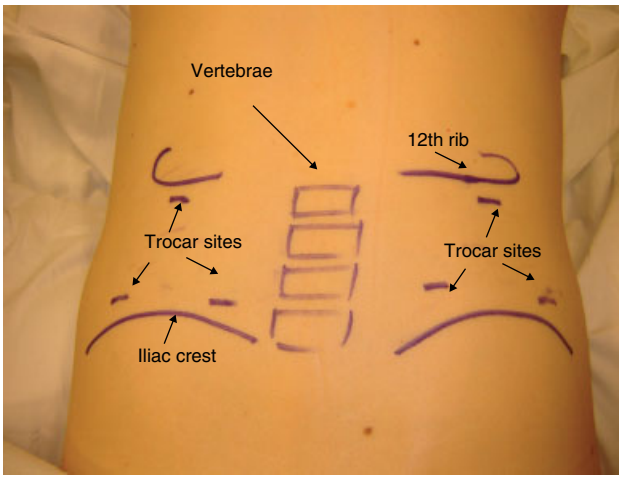

Fig. 1 Trocar sites and anatomical landmarks for bilateral retroperitoneal endoscopic adrenalectomy

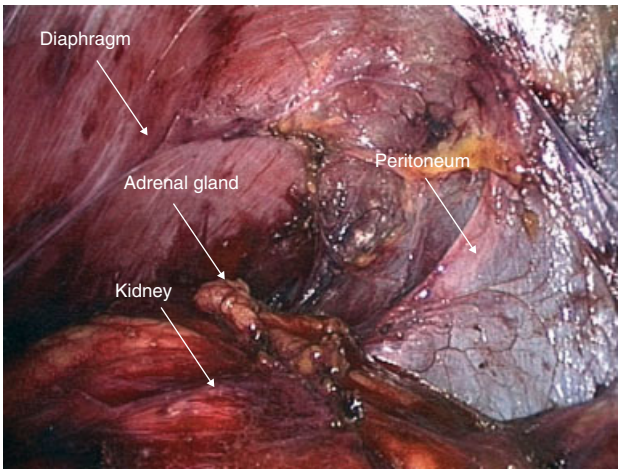

Fig. 2 Endoscopic view of operative field for retroperitoneal endoscopic adrenalectomy on the left side

(Covidien). The surgical site was checked for haemostasis and the trocars were removed under endoscopic view. The muscle fascia was closed and the skin was closed intracutaneously. No drains were used.

Statistical analysis

Continuous data were reported as mean(s.d.) (range) or median (interquartile range) depending on the distribution, as tested by a histogram. Operating times were studied for a possible learning curve. SPSS® version 16.0 (SPSS, Chicago, Illinois, USA) was used for statistical analysis.

Results

Between October 1997 and December 2008, 112 REAs were performed in 105 patients. Seven patients underwent bilateral adrenalectomy. In five patients, a subtotal adrenalectomy was carried out to preserve adrenal gland function. These patients had multiple endocrine neoplasia type 2 with either unilateral or bilateral phaeochromocytoma. Patient characteristics are shown in *Table 1*. The mean age was 46(15) (9–74) years. Four patients underwent REA for solid tumours larger than 6 cm. In none of these patients was it clear on preoperative imaging that the tumour was larger than 6 cm. Two of them had an ACTH-producing neuroendocrine tumour causing bilateral adrenal hyperplasia, which led to uncontrollable hypercortisolism. During the same interval, 44 conventional open adrenalectomies were performed. Indications for these open procedures were tumour larger than 6 cm or a suspected primary adrenal malignancy (adrenocortical carcinoma). One patient had a robot-assisted adrenalectomy. Details of these procedures were not studied further.

Operative data are summarized in *Table 2*. The median duration of unilateral operations was 100 (90–130) min.

Table 1 Characteristics of 105 patients undergoing retroperitoneal endoscopic adrenalectomy

	No. of patients*
Left : right	65 : 40
Unilateral : bilateral	98 : 7
Subtotal adrenalectomy	5
Tumour size (cm)†	3·1 (2·0–4·4)
Body mass index (kg/m^2)†	27 (23–29)
Indications: unilateral operation	
Phaeochromocytoma	39
MEN2A	15
MEN2B	1
Von Hippel–Lindau disease	1
SDHD mutation	2
Cushing's disease (ACTH independent)	21
Conn's disease	20
Testosterone-producing tumour	1
Incidentaloma	12
Suspected metastasis‡	2
Other/non-functioning tumour	3
Indications: bilateral operation	
Cushing's disease (ACTH dependent)	5
Phaeochromocytoma (MEN2A)	2

*Unless indicated otherwise; †values are median (interquartile range). ‡Of two suspected metastases, only one was proven to contain malignancy on final histology of a clear cell renal carcinoma. MEN, multiple endocrine neoplasia; SDHD, succinate dehydrogenase complex subunit D; ACTH, adrenocorticotrophic hormone.

Table 2 Operative details

	No. of patients*
Duration of unilateral operation (min)†	100 (90–130)
Left adrenalectomy	100 (90–132)
Right adrenalectomy	115 (90–130)
BMI < 25 kg/m^2	90 (90–121)
BMI 25–30 kg/m^2 (overweight)	106 (90–150)
BMI > 30 kg/m^2 (obese)	120 (90–133)
Duration of bilateral operation (min)†	175 (150–300)
Blood loss (ml)†	5 (0–50)
Conversion	2
Postoperative hospital stay (days)†	3 (2–5)
Postoperative complications	
Severe	2
Mild	5
Late complications	
Persistent hypertension	7
Chronic pain symptoms	3
Death	0

*Unless indicated otherwise; †values are median (interquartile range). BMI, body mass index.

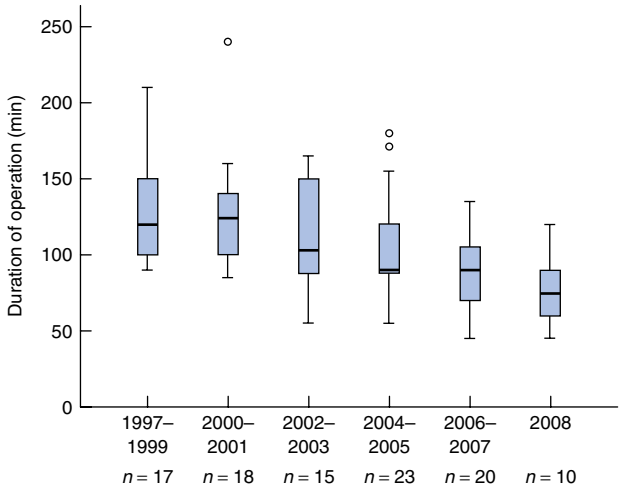

Fig. 3 Learning curve for retroperitoneal endoscopic adrenalectomy. Mean duration of operation is plotted against time interval. Median values, interquartile ranges and ranges (excluding outliers; ∘) are represented by horizontal bars, boxes and error bars respectively

After 30 procedures the median operating time had decreased significantly from 120 (100–140) to 90 (88–120) min ($P = 0{\cdot}042$). After 40 procedures a further decrease was seen over time (*Fig. 3*). A body mass index of 30 kg/m^2 or more did not appear to affect the duration of operation significantly ($P = 0{\cdot}706$).

Two conversions (1·8 per cent) to open conventional surgery were necessary owing to an insufficient view of the operative field. There were no perioperative deaths. During the operation, six patients with phaeochromocytomas developed systolic blood pressures of 200 mmHg or more despite α- and β-blockade. After operation, one patient required re-exploration for persistent bleeding from the muscular part of a trocar insertion site. Another patient developed congestive heart failure, which was successfully treated conservatively. Minor complications occurred in five patients, including flank haematoma and superficial wound infection. Median hospital stay was 3 (2–5) days.

Final histology of 12 patients with an incidentaloma led to a diagnosis of seven adenomas, one case of hyperplasia, one phaeochromocytoma, one myelolipoma, one haematoma and one normal adrenal gland. Apart from one renal cell carcinoma metastasis, none of the tumours was confirmed to be malignant at final histology.

During follow-up three patients complained of wound pain, which eventually subsided. Two other patients developed bulging of the flank wall (diastasis). Seven patients had persistent hypertension after REA, six of whom had Conn's disease before surgery. However, although exact levels had not been documented, hypertension in all six patients was noted as improved after operation. None of the patients had persistent hypokalaemia.

None of the patients developed signs of malignant disease during follow-up, including one who had a testosterone-producing tumour. During follow-up of 1 year, the patient with renal cell carcinoma metastasis did not develop new metastatic disease. One of two patients with a neuroendocrine ACTH-producing tumour died from metastatic disease from the neuroendocrine tumour 3 years after bilateral adrenalectomy (adrenal hyperplasia greater than 6 cm).

Discussion

Based on this review of 112 REAs in a single centre, the procedure appears to be a safe and effective approach for the majority of adrenal tumours. Similar to the experience of Walz and colleagues with posterior retroperitoneoscopy, no 'collateral' damage to other/adjacent organs was observed[19]. REA was associated with minimal blood loss, very low conversion and morbidity rates, and no deaths. A steady learning curve showed a significant decrease in operating time from 120 min for the earliest procedures to 90 min more recently.

Most centres use the transabdominal approach for adrenalectomy[4,8,10–14,16,23–27], which provides good exposure and anatomical landmarks. On the other hand, in addition to the advantage of a smaller risk of collateral organ damage, REA is not impeded by adhesions caused by previous abdominal surgery. Furthermore, for removal of bilateral adrenal tumours, the patient is already in the jack-knife position and does not have to be repositioned, thus reducing total operating time[21].

The number of complications in present series was small (1·8 per cent major, 6·3 per cent total). In comparison, overall complication rates in transabdominal series have been reported to range from 3 to 20 per cent[3]. Bleeding is the most common complication following transabdominal adrenalectomy. Organ injury (liver, spleen, kidney, large bowel and diaphragm) occurs in around 4 per cent[3]. Incisional hernia is common following the transabdominal approach (10 per cent), whereas port-site hernias are rare after REA[17].

Conversion to open surgery was required in two of 112 procedures, similar to published conversion rates (2–3 per cent)[7,11,13,21]. Persistent hypertension was found in seven patients after the operation, six of whom had Conn's disease, but an improvement in hypertension was noted in these six patients. Persistent hypertension after adrenalectomy in patients with Conn's disease has

been described previously, with rates varying from 0 to 25 per cent. This phenomenon is most likely caused by pre-existing essential hypertension[8,11].

Although REA was successful in morbidly obese patients, difficulties were sometimes encountered in obtaining good exposure and insufflating the retroperitoneal space. Others have also found that high intracavitary pressures of up to 20–24 mmHg may be necessary to obtain good exposure[20,21]. Although this may lead to increased central venous pressure, arterial pressure and cardiac output, such problems were not encountered in this and other series[20,21,28]. Major bleeding complications were not observed. However, should bleeding occur from the inferior vena cava, the limited space may make it difficult to control. Therefore, careful dissection with a smooth instrument (such as a suction device) is recommended in the vicinity of the adrenal vein.

Endoscopic adrenalectomy has been advocated particularly for tumours up to 6 cm in size. For larger tumours, carrying a higher risk of malignancy, open resection is more often favoured. Nonetheless, larger tumours have been resected endoscopically, predominantly using the transabdominal approach[3,23,26,29]. In the present series, tumours of up to 7·5 cm were removed occasionally without problems. It is obvious that locally invasive growth has to be excluded on preoperative imaging in such circumstances[20,21].

Although it is standard practice to remove the entire adrenal gland, a subtotal adrenalectomy can be carried out[7,11,21] in order to preserve adrenal function in patients with bilateral adrenal tumours or at increased risk of developing a contralateral phaeochromocytoma (for example those with familial syndromes such as multiple endocrine neoplasia type 2 and von Hippel–Lindau disease). In the present series, five subtotal adrenalectomies were performed successfully. Tumours smaller than 2 cm and located peripherally are most suitable for this technique, which is technically not difficult. To preserve adrenal function, approximately one-third of the adrenal gland must be left *in situ*[7,30].

The duration of operation in the present series was shorter than that reported for the transabdominal approach[3,10,31]. Walz and colleagues[21] demonstrated a learning curve for the retroperitoneal endoscopic approach, with a decrease in operating time to 40 min after 560 procedures. In light of these findings, in combination with the relative rarity of the disorder, centralization of this type of surgery is recommended. In addition, a team consisting of the same surgeons, anaesthetists and operating nurses is advocated.

The main limitation of this study is the retrospective and uncontrolled setting, making a sound comparison between different techniques difficult. However, owing to the relatively low prevalence of the disease, it is unlikely that sufficiently large randomized trials will be accomplished.

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Commentary

Retroperitoneal endoscopic adrenalectomy is safe and effective (*Br J Surg* 2010; 97:1667–1672)

Open adrenalectomy may be performed via a transperitoneal, retroperitoneal or thoracoabdominal approach. Laparosopic transabdominal adrenalectomy (LTA) was introduced in 1992[1], and soon became the standard of care at select institutions for most functional and non-functional tumours of the adrenal. Because the adrenals are located in the posterior retroperitoneum, however, a posterior endoscopic approach provides more direct access, albeit in a more limited space. Retroperitoneal endoscopic adrenalectomy (REA) was popularized by Walz and colleagues[2], who have demonstrated excellent results in large series with various underlying pathology[3]. In this issue of *BJS*, the group led by Professor Borel Rinkes describes a single-institution experience of 112 REAs for benign adrenal tumours over an 11-year period (1997–2008). Overall, the results are excellent with low rates of morbidity and no deaths, similar to other studies of REA and LTA. The median duration of operation was less than 2 h and the median blood loss negligible (5 ml). There were two major (postoperative bleeding requiring reoperation and congestive heart failure) and five minor (flank

haematoma and surgical-site infection) complications. Two patients required conversion from REA to an open procedure. Flank wall herniation developed in two patients during postoperative surveillance.

REA has been further established as an effective and safe surgical alternative to LTA for adrenal tumours. Although not investigated explicitly in this study, REA may indeed have some advantages over LTA, especially in the setting of previous intra-abdominal operations, obesity and bilateral adrenal neoplasms. The major disadvantage relates to the more limited working space, making REA challenging for large tumours.

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