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ORIGINAL ARTICLE

Laparoscopic adrenalectomy for adrenal tumors: A 21-year single-institution experience

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Summary *Objective:* We have performed laparoscopic adrenalectomy including retroperitoneoscopic adrenalectomy via a single large port (RASLP) and conventional laparoscopic adrenalectomy (CLA) for adrenal tumors since 1992, and report our experience to date.
Methods: The study population consisted of 134 patients who underwent laparoscopic adrenalectomy from 1992 to 2012. Fifty-eight patients (18 aldosterone-producing adenomas, 13 adenomas with Cushing's syndrome, 1 adenoma with preclinical Cushing's syndrome, and 26 nonfunctioning tumors) were treated using RASLP, and 76 patients (33 aldosterone-producing adenomas, 17 adenomas with Cushing's syndrome, 6 adenomas with preclinical Cushing's syndrome, 17 pheochromocytomas, and 3 nonfunctioning tumors) were treated using CLA. Complications were graded according to the modified Clavien system.
Results: The majority of RASLPs were performed during the 1990s, whereas all patients underwent CLA after 2000. The mean operation times (166 vs. 205 minutes, $p < 0.01$) and intraoperative estimated blood loss (85 vs. 247 mL, $p < 0.01$) were significantly lower in the CLA group. Conversion to open surgery was required in three patients (5%) in the RASLP group and five patients (7%) in the CLA group ($p = 0.73$). Postoperative complications were grade

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1 in three patients and grades 4 and 5 in one patient each in the RASLP group, whereas grade 2 in one patient was observed in the CLA group ($p = 0.085$).
Conclusion: Although this study included biases such as different eras and indications, CLA resulted in decreased operative times, blood loss, and postoperative complications compared with RASLP. CLA has so far become our preferred procedure for patients with adrenal tumor in our experience.

1. Introduction

In 1985, Buess et al[1] performed endoscopic surgery of the rectum using a rectoscope 4 cm in diameter and with a large working lumen. We first performed retroperitoneoscopic adrenalectomy via a single large port (RASLP) using this wide-lumen rectoscope to treat a small adrenal tumor without carbon dioxide insufflation in 1992.[2] We subsequently performed RASLP routinely, reporting the techniques involved and outcomes in 2005.[3] Our unique procedure introduced a template for the development of laparoendoscopic single-site surgery (LESS),[4] which has seen increasing uptake recently with advancements in surgical instruments, greater consideration of cosmetics, and the trend towards minimal invasiveness. Indeed, there has been a paradigm shift in the field of minimally invasive surgery, as laparoscopy progresses towards scar-free techniques. Although different techniques and devices have been reported in the published data on surgery with various terminologies and acronyms applied, natural orifice translumenal endoscopic surgery[5] and LESS[6] are emerging in an effort to duplicate standard laparoscopic procedures through a virtually scar-free approach.

By contrast, since the introduction of the laparoscopic approach to adrenalectomy in 1992 by Gagner et al,[7] this minimally invasive technique has gained worldwide acceptance and has become the gold standard for the removal of most small, benign lesions of the adrenal gland as conventional laparoscopic adrenalectomy (CLA) including lateral transperitoneal and retroperitoneal approaches. We have also performed CLA routinely for adrenal tumors including even relatively large tumors and pheochromocytoma since the year 2000. The purpose of this study was to evaluate our single-center experience with RASLP and CLA performed for a variety of adrenal tumors.

2. Materials and methods

We reviewed the records of all patients undergoing laparoscopic adrenalectomy at our institution (Nihon University Itabashi Hospital, Tokyo, Japan) from May 1992 to December 2012. Data were extracted from institutional review board-approved databases. Data extracted included patient age, sex, body mass index (BMI), operative history, tumor size, side effects of disease, and characteristics on imaging and clinical diagnosis. In addition, information relating to the perioperative course such as operative time, estimated blood loss, conversion to open surgery, perioperative mortality, complications, postoperative hormonal prognosis in functioning tumors, and tumor recurrence was extracted from the operative notes, anesthesia records, and inpatient and outpatient charts.

RASLP was indicated for unilateral and small benign adrenal tumors (<4.5 cm in diameter) excluding pheochromocytoma, whereas CLA was indicated for all benign adrenal tumors with the exception of those with malignant potential. Surgical indication of nonfunctioning adrenal tumors after 2003 was according to the consensus conference on the topic at the National Institute of Health in 2002.[8]

The surgical technique of RASLP has been previously described in detail.[3] Briefly, patients were placed in the lateral decubitus position with slight flexion, and a 4.5-cm skin incision was made below the 12th rib in the mid axillary line. The retroperitoneal space was dissected using index fingers and a balloon dilator. A rectoscope tube (4 cm in diameter) was inserted, and the adrenal glands were endoscopically removed via the single large port without carbon dioxide insufflation. Figure 1 shows an operating scene including a tube of rectoscope inserting into the retroperitoneal space and a retroperitoneoscopic finding, and postoperative scar.

CLA including transperitoneal lateral and retroperitoneal lateral approaches were performed using standard techniques with small modifications routinely using multiple ports and carbon dioxide insufflation.[9] In the transperitoneal approach, the primary port site was located at the lateral margin of the ipsilateral rectus muscle at the level of the umbilicusor several fingerbreadths above the umbilicus. Secondary ports were placed in the anterior axillary line/ipsilateral rectus near the costal margin. An auxiliary port was necessary for retraction of the liver on the right side (Figure 2). The abdominal cavity was insufflated to 8—12 mmHg using carbon dioxide. On the left side, the renal hilum was directly approached to expose the renal vein. The adrenal vein was identified on its cranial surface and ligated. On the right side, the inferior vena cava was identified and traced up to the gland that was dissected primarily prior to ligating the short adrenal vein as it enters the vena cava. All specimens were retrieved within an endoscopic pouch through the primary port. In the retroperitoneal approach, an initial port was made near the tip of the 12th rib under the 11th rib, and the retroperitoneal space was extended with balloon distension. After carbon dioxide insufflation of the retroperitoneum, the other trocars were placed at the angle of the paraspinal muscle and the origin of the 12th rib, and approximately

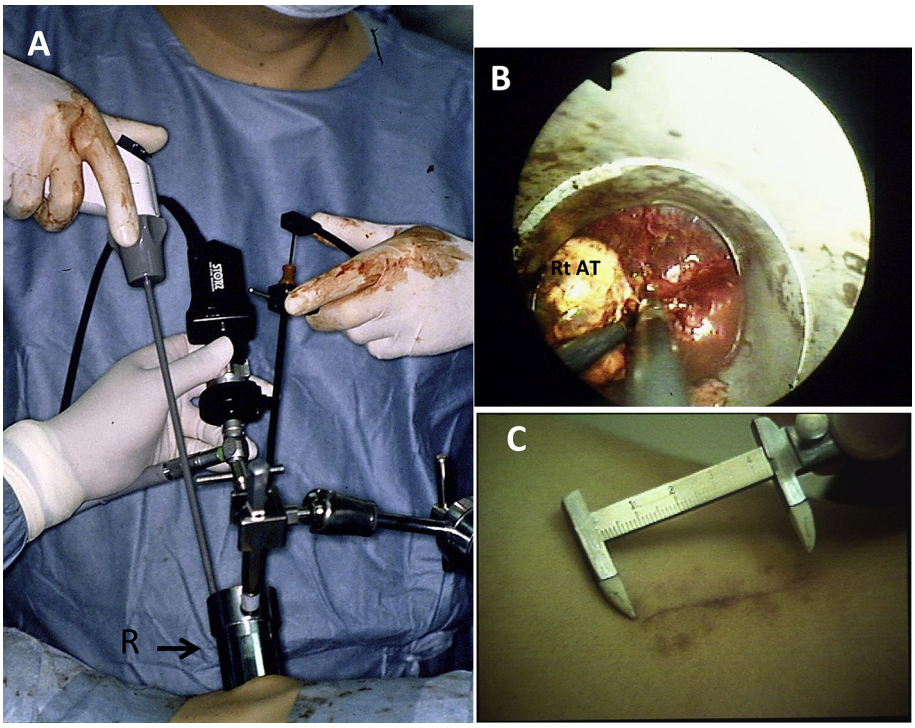

Figure 1 (A) Insertion of rectoscope tube into the retroperitoneal space; (B) retroperitoneoscopic finding; and (C) postoperative scar from retroperitoneoscopic adrenalectomy via a single large port. R = rectoscope tube; RtAT = right adrenal tumor.

two fingerbreadths above the iliac crest near the anterior superior iliac spine. Then the procedures were carried out in a similar manner to previous reports.[9] Our series was mostly confined to expert operators in the CLA procedure but was unconfined in the RASLP. Postoperative complications were graded according to the modified Clavien system published in 2004.[10]

Demographic, clinical, and perioperative outcomes including complications were compared for the two groups using the Fisher exact test and the Mann—Whitney *U* test. StatView software (Abacus Concepts, Inc., Berkeley, CA, USA) was used for all statistical analyses. All calculated *p* values were two sided, and those <0.05 were considered statistically significant.

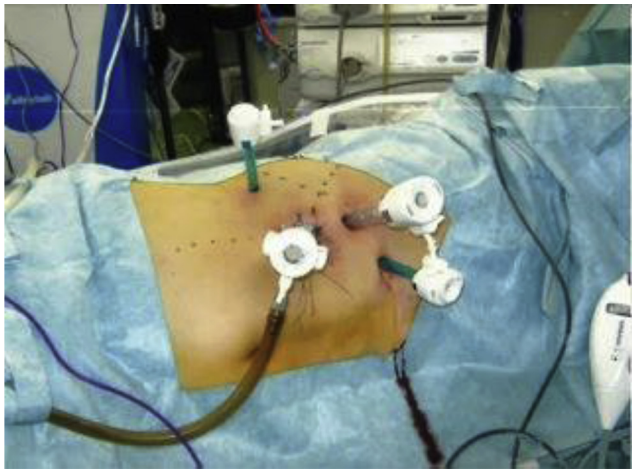

Figure 2 Placement of trocars for conventional transperitoneal laparoscopic right adrenalectomy.

3. Results

In the past 21 years, 134 laparoscopic adrenalectomies have been performed on 134 patients with adrenal tumor. Of these patients, 58 underwent RASLP and 76 received CLA (67 transperitoneal lateral and 9 retroperitoneal lateral approaches). The majority of RASLP treatments were performed during the 1990s, whereas all patients underwent CLA after 2000 (Figure 3). Table 1 details the patient and disease characteristics. The distributions of age, sex, BMI, tumor location, and tumor size were similar between the two groups. In preoperative clinical diagnosis, the RASLP group included a large number of nonfunctioning tumors (45%) because of the lack of consensus for management of patients with nonfunctioning adrenal tumors when performing the RASLP prior to 2002, whereas the CLA group included 17 (22%) pheochromocytomas. The histological evaluation demonstrated that all of the functioning and preclinical Cushing's syndrome tumors except for pheochromocytoma, across both groups, were adrenocortical adenomas. The nonfunctioning tumors comprised 20 cases of adrenocortical adenoma, and one case each of nodular hyperplasia, pseudocyst, hemorrhagic cyst, ganglioneuroma, myelolipoma, and a metastatic tumor from lung cancer in the RASLP group, and one case each of bronchogenic cyst, cystic lymphangioma, and myelolipoma in the CLA group.

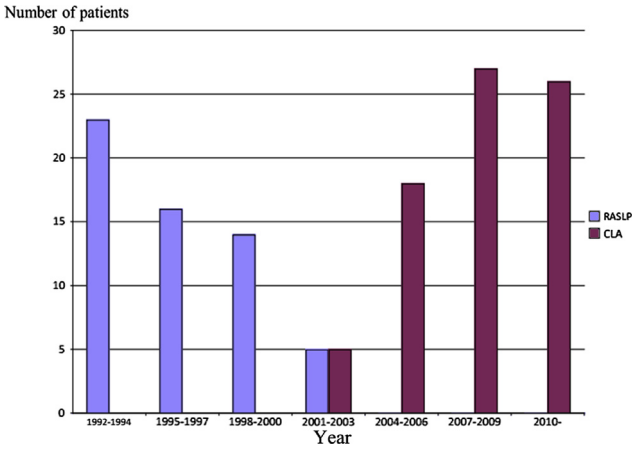

Figure 3 Number of RASLP and CLA in generation distinction. The majority of RASLP treatments were performed during the 1990s, whereas all patients underwent CLA after 2000. CLA = conventional laparoscopic adrenalectomy; RASLP = retroperitoneoscopic adrenalectomy via a single large port.

Table 2 lists the intraoperative results. Operative time (mean 166 vs. 205 minutes, $p < 0.01$) and intraoperative estimated blood loss (mean 85 vs. 247 mL, $p < 0.01$) in the CLA group were significantly decreased compared to those in the RASLP group, whereas the population of conversion to open surgery was lower in the RASLP group; however, the difference between the groups was not statistically significant ($p = 0.73$). Of the patients converted to open surgery, two patients in the RASLP group experienced bleeding requiring blood transfusion and one patient with Cushing's syndrome had an unidentified tumor due to excessive retroperitoneal fat. In the CLA group, conversion to an open surgery was required in five patients owing to bleeding in one, adhesion to periadrenal adipose tissue and the vena cava in three, and no identification of tumor in the remaining case. An intraoperative outcome analysis between transperitoneal and retroperitoneal approaches found no significant difference between these CLA subgroups in the evaluated factors including operative time, intraoperative estimated blood loss, and conversion to open surgery.

Overall, intra- and postoperative complications (Table 3) were observed in 14 patients (10%). Intraoperative complications in the RASLP group included grade 2 (hemorrhage) in four patients (7%), and grade 3 (pneumothorax) in three patients (5%) during dissection of the retroperitoneal space using a balloon dilator and fingers, whereas only one patient (1%) in the CLA group experienced grade 2 due to bleeding ($p = 0.02$). Postoperative complications in the RASLP group included grade 1 (superficial wound infection) in three patients (5%) with Cushing's syndrome, grade 4 (pulmonary thrombosis) in one patient (2%) with primary aldosteronism that was complicated by presurgery atrial fibrillation, and grade 5 (death) in one patient (2%) with preclinical Cushing's syndrome who had postoperatively fulminant hepatitis. In contrast, only one patient (1%) in the CLA group experienced grade 2 (ileus) in the postoperative complications. No statistically significant difference was found between the groups ($p = 0.08$).

Table 1 Patient characteristics.

	RASLP	CLA	*p*
No. of patients	58	76	
Age (y), m ± SD	50 ± 10	48 ± 15	0.53
Sex			0.72
Male	20	29	
Female	38	47	
BMI, m ± SD	23.9 ± 3.5	23.6 ± 3.6	0.64
Clinical diagnosis			<0.01
APA	18	33	
Cushing's syndrome	13	17	
Pre-Cushing's syndrome	1	6	
Pheochromocytoma	1	7	
Nonfunctioning tumor	26	3	
Tumor location			0.86
Right	30	37	
Left	28	39	
Tumor size (cm), m ± SD	2.6 ± 1.1	2.7 ± 1.2	0.95

APA = aldosterone-producing adenoma; CLA = conventional laparoscopic adrenalectomy; RASLP = retroperitoneoscopic adrenalectomy via a single large port; SD = standard deviation.

Table 2 Intraoperative outcomes.

	RASLP	CLA	*p*
Operative time (min), mean ± SD	205 ± 57 (range 92–320)	166 ± 60 (range 68–442)	<0.01
Intraoperative estimated blood loss (mL), mean ± SD	247 ± 293 (range 10–1700)	85 ± 198 (range 3–600)	<0.01
Conversion to open surgery	3 (5%)	5 (7%)	0.73

CLA = conventional laparoscopic adrenalectomy; RASLP = retroperitoneoscopic adrenalectomy via a single large port; SD = standard deviation.

Table 3 Intra- and postoperative complications according to the modified Clavien system.

	RASLP	CLA	*p*
Intraoperative complications, *n* (%)			0.02
Grade 2	4 (7)	1 (1)	
Grade 3	3 (5)		
Postoperative complications, *n* (%)			0.08
Grade 1	3 (5)		
Grade 2		1 (1)	
Grade 4	1 (2)		
Grade 5	1 (2)		

CLA = conventional laparoscopic adrenalectomy; RASLP = retroperitoneoscopic adrenalectomy via a single large port.

In terms of postoperative hormonal prognosis and tumor recurrence, all patients with functioning adrenocortical adenoma or pheochromocytoma showed normal function with no tumor relapse at a median follow up of 40 months.

4. Discussion

Adrenal surgery rates have been increasing in conjunction with the increased prevalence of incidental adrenal masses found on routine cross-sectional imaging.[11] Simhan et al[12] reported that the mean number of adrenal procedures performed per hospital with time increased from a mean number of 2.9 in 1996 to 5.5 in 2009 based on data in the northeastern United States (New York, New Jersey, and Pennsylvania), and a shift was noted from very low volume hospital to very high volume hospital in the proportion of patients who underwent adrenal surgery. In our institution, the average number of endoscopic adrenalectomies performed was 6.4 per year, and recently this figure has increased.

Endoscopic adrenalectomies, including the transperitoneal lateral and retroperitoneal lateral approaches, are currently the standard procedures used for treating adrenal tumors. However, both conventional laparoscopic approaches require several ports and carbon dioxide insufflation to obtain a working space. As we have previously described,[3] RASLP does not require carbon dioxide and provides direct exposure to the adrenal gland, and permits the removal of large tumors without fraction as long as they are smaller than the diameter of the large port. However, RASLP has major disadvantages including the relatively wide skin incision compared with that in hand-assisted laparoscopic procedures, a smaller working space, and interference of instruments in the dissection compared with CLA. The most important technical factor for conducting the RASLP operation is the act of placing the rectoscope tube appropriately in the center of the dissecting area and pressing the periadrenal adipose tissues and surrounding organs with the tube. Thus, this procedure is not appropriate for obese patients or for the treatment of pheochromocytoma. In addition, there were no contemporary devices used for LESS surgery when performing RASLP, and these major disadvantages resulted in decreasing the number of RASLPs performed in the following years; we have also shifted from RASLP to CLA for all adrenal tumors that were indicated for laparoscopic surgery since 2004.

The operative time and intraoperative estimated blood loss were markedly decreased in the CLA group compared with the RASLP group. The larger operative field of the conventional transperitoneal approach helps to better orientate and visualize familiar landmarks known from open surgery. During treatment of adrenal tumors using the CLA techniques, developed contemporary devices such as bipolar vessel sealing device (Ligasure, Valleylab, Boulder, Colorado, USA) and ultrasonic coagulating shears were used in the majority of cases. CLA offers several advantages. In the CLA group, the duration of surgery and estimated blood loss in the initial 20 cases were significantly increased compared to those in the subsequent 56 cases. However, the operative time and estimated blood loss in the initial 20 cases were similar to those in the subsequent cases in the RASLP group because of undefined expert operators, as previously described.[3]

An extensive review undertaken by Brunt[13] indicated that 37 of 1083 patients (3.4%) underwent conversions to open adrenalectomy during CLA, based on a meta-analysis. Shen et al[14] demonstrated that significant independent predictive factors for conversion to open surgery were tumor size of $\geq$5 cm, BMI of $\geq$24 kg/m^2, and pheochromocytoma based on multivariate analysis. In our study, the rates of conversion to open surgery were high, especially in the CLA group, although all such cases in the CLA group were experienced in the earlier learning curve, and comprised three pheochromocytomas and one case each of aldosterone-producing adenoma and cystic lymphagioma. Catecholamine-induced hypertension occurred during dissection in patients with pheochromocytoma in whom the transperitoneal lateral approach was converted to open surgery, and their tumors were relatively enlarged (5—7 cm) and were adherent to periadrenal adipose tissues. Treatment of relatively enlarged pheochromocytoma should therefore be avoided even when using conventional transperitoneal laparoscopic procedures in the early learning curve phase. The patient with histologically cystic lymphangioma who underwent CLA using the retroperitoneal lateral approach was converted to open surgery because there was no identifiable tumor.

Early complications rates of 0—15% in laparoscopic adrenalectomy have been reported.[15] General complications associated with laparoscopic adrenalectomy include wound hematomas and infection, and deep vein thrombosis. Patients with Cushing's syndrome are more prone to infectious and thrombotic complications. Specific complications include injury to surrounding organs such as the liver, pancreas, spleen, inferior vena cava, renal vessel, diaphragm, and pleura. In this study, there were significantly fewer perioperative complications in the CLA group than the RASLP group. Only one patient (1%) experienced grade 2 complication (bleeding requiring blood transfusion) in the CLA group, whereas 12 patients (21%) in the RASLP group showed complications with two (3%) of these patients experiencing grade 4 and grade 5 postoperative complications such as pulmonary thrombosis and fulminant hepatitis. CLA procedures are superior to RASLP procedures with respect to intra- and postoperative complication rates.

However, despite being an evolution of the standard laparoscopic surgery, LESS recently defied the most basic tenets of laparoscopy including triangulation of working instruments and external spacing to decrease intra- and extracorporeal clashing,[16] and several multichannel platforms have been developed for LESS in urological surgery.[17] The development of articulating and bent instrumentation permits triangulation intracorporeally despite the close proximity of several instruments via a single port. Cindolo et al[18] reported the first case of LESS transperitoneal adrenalectomy using such purpose-built instruments such as the Triport (Olympus, Tokyo, Japan) and articulated instruments. In their procedures, the Triport was inserted through a 3-cm subcostal incision with carbon dioxide insufflation of the abdomen. By comparison, our RASLP procedures involved a rectoscope tube (4 cm in diameter) being inserted through a 4.5-cm skin incision without carbon

dioxide insufflation, resulting in a slightly longer incision. The operative time and blood loss in the reported LESS adrenalectomy were 240 minutes and 20 mL, respectively. The operative time was similar in our RASLP patients; however, they experienced less blood loss. This could be attributed to the use of carbon dioxide insufflation during their operation. Jeong et al[19] reported the first study comparing LESS adrenalectomy and CLA in the treatment of benign adrenal adenomas, and their results showed no significant differences in mean operative time, blood loss, and postoperative hospital stay between the LESS and CLA groups. The authors concluded that LESS adrenalectomy for benign adrenal adenoma is comparable to the conventional laparoscopic approach in terms of perioperative parameters, but with more desirable cosmetic outcomes. However, in LESS no proven or documented benefits except for cosmetic advantage exist over the conventional approach, and only experienced laparoscopic surgeons should attempt this technique in clinical settings according to the European Association of Urology guidelines on robotic and single-site surgery in urology.[20] We did not use the same contemporary devices for LESS surgery when performing RASLP. Even with the use of developed contemporary instruments, RASLP is likely to be inferior to LESS surgery because the working space is smaller in the RASLP as carbon dioxide insufflation is not used.

In conclusion, although this study was based on retrospective analysis with different eras and indications for patients treated with RASLP versus CLA, the perioperative outcomes measured in the RASLP group were inferior to those in the CLA group. CLA has so far become our preferred procedure for patients with adrenal tumor.

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