Lateral retroperitoneoscopic adrenalectomy for complicated adrenal tumor larger than 5 centimeters.

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Abstract

Background: The role of lateral retroperitoneoscopic adrenalectomy (LRA) for complicated tumor with large diameter remains controversial, this study aimed to evaluate the effectiveness of this procedure on the management of tumor larger than 5cm in diameter.

Methods: A retrospective comparison was conducted of 67 patients with large complicated adrenal tumor (>5cm). 41 patients received LRA, and 26 received open adrenalectomy (OA) in our hospital between January 2011 and June 2015. Basic characteristics regarding mean age, gender, body mass index (BMI), tumor size, tumor side, previous abdominal surgery, resection method, pathology were preferentially analyzed. Operative indicators regarding operation time, estimated blood loss (EBL), conversion to ICU, complications, post-operative hospitalization, duration of drain, time to first oral intake and ambulation were compared between groups.

Results: There were no significant differences between the two groups in the basic characteristics. The mean operation time for LRA was shorter than OA (98.7±32.3 min vs 152.7±72.3 min, P = 0.001). EBL was 31.9±20.0 ml for LRA and 590.0±1181.1 ml for OA (P = 0.03). There was no complication in LRA group and one patient in OA group had complications, but this difference was not significant (P = NS). The post-operative hospitalization in LRA was 7.4±2.8 days, and shorter than 9.8±2.7 days in OA group (P = 0.00). The time to first oral intake and ambulation for LRA was shorter than OA (first oral intake, 1.9±0.8 days vs 3.1±1.3 days, P = 0.00; time to ambulation, 2.6±1.4 days vs 4.2±1.6 days, P = 0.00). While the difference between groups were not significant in terms of ICU conversion (3/41 vs 4/26, P = NS) and duration of drain (3.9±2.2 days vs 4.7±1.9 days, P = NS).

Conclusion: Our study shows that LRA can be performed safely and effectively for complicated adrenal tumors larger than 5 cm in diameter, but it remains technically demanding.

Keywords: Retroperitoneoscopic adrenalectomy; adrenal tumor; lateral position.

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Introduction

Since the endoscopic technique was first introduced to perform adrenalectomy in 1992, several approaches of laparoscopic adrenalectomy have been widely used in the treatment of the vast majority of benign adrenal tumors. Among the various approaches, the retroperitoneoscopy was widely accepted due to the direct vision. While due to the limited space of posterior peritoneum, the indications of this approach was also confined to small adrenal tumors.

Satisfactory clinical results of lateral retroperitoneoscopic adrenalectomy (LRA) have been reported in small adrenal tumors, while there is a paucity of data on the large or malignant adrenal tumors. In the last decades of 20th century, Henry presented a successful case series of patients who received retroperitoneoscopic adrenalectomy, with potential malignant and large diameter adrenal tumors. However, different opinion has existed in some surgeons. Due to the narrow working space, many scholars tend to choose an open or transperitoneal approach to deal with large adrenal tumors.

The aim of this study was to compare the operative outcome of LRA versus open surgery in the treatment of patients with large diameter (≥ 5cm) complicated adrenal tumors.
Patients and methods
The prospectively maintained urology database in the department of urology at Zigong No.4 people’s hospital was retrospectively reviewed to collect data on the large diameter complicated adrenal tumor patients who underwent LRA or open surgery, from January 2011 to June 2015. There were 67 patients with adrenal tumor larger than 5cm. Of the 67 cases, 41 (26 male and 15 female) underwent LRA and the other 26 (13 male and 13 female) underwent open procedure. All of the patients received complete laboratory examination, which involved plasma metanephrines, aldosterone, renin and the aldosterone/renin ratio (ARR), vanilmandelic acid (VMA), 17-hydroxycorticosteroids (17-OHCS), and 17-keto-steroid (17-KS). Image evaluations such as computed tomography (CT) were used to determine the localization and diameter of adrenal mass. Open surgery was used in patients with local lymph invasion or periadrenal involvement according to the radiographic evidence. All of the patients were provided operative informed consent, which mentioned the benefits and potential risks of proposed operation method. For patients proposed to LRA, we also informed them that the open conversion might be chosen once any difficulties were encountered during the operation.

Surgical technique
According to the different surgical methods, all the patients were divided into LRA group and open adrenalec-tomy group (OA). A 30-degree laparoscope was used as observation mirror though a 10 mm trocar, the other two trocars were located in anterior axillary line and posterior axillary line of subcostal space with a diameter in 5 mm or 10 mm (Figure 1).

Ultrasound shears were used to divide and identify the edge of adrenal gland. The adrenal central vein was divided between hem-o-lok clips. After the adrenal was dissected completely, a self-made bag was used to dress up the adrenal gland via a 10 mm trocar into the peritoneal cavity. The mass was cut and examined on the operation table to ensure the entire tumor was involved. If it is necessary, a hand-assisted retroperitonoscopic adrenalectomy (HARA) was used in the LRA group, which was placed at the intersection of mid-axillary line and subcostal area (Figure 2).
After the adrenal area was exposed, special attention would be given to evaluate the tumor location and whether there is periadrenal involvement. In both the LRA and OA group, the main principle was resection with as much peri-adrenal tissue as possible to ensure the highest negative margin rate. Drainage tube was routinely placed before operation was complete. All the procedures were performed by senior experienced laparoscopic surgeons to reduce the selective bias.

Post-operative management
Routinely, the patients were put in the post-anesthesia care unit (PACU) until the blood pressure and heart rate were stable, and the patients had regained consciousness after surgery. Patients with significant bleeding or labile blood pressure were converted to intensive care unit (ICU). After approximately thirty minutes’ post-operative monitoring in PACU, patients were transferred to urology department for half to one day’s electrocardiography monitoring. 24 hours to two days’ fasting was needed to help the bowel function recovery. During this period, post-operative intravenous fluid supplement was used in all the patients. Post-operative hypotension would be timely corrected, and this could have been caused by the bleeding or inadequate intravenous fluids supplement during the intra- or post-operative; fortunately, there was no patient who required this management. Patients were discharged after adequate pain control and the drainage tube was extubated. In addition, patients received regular diet and normal ambulation as regards to the requirement condition to achieve discharge standard.

Outcome definition
To evaluate the efficacy of LRA and OA, both the intra-operative terms and post-operative terms were needed. The intra-operative terms included; operation time, estimated blood loss (EBL), complications and number of ICU conversions. The post-operative terms included; hospitalization, duration of drain, time to first oral intake and time to first ambulation.

Additionally, basic characteristics was preferentially analyzed to assess the balance and comparability between two groups, which covered mean age, gender, body mass index (BMI), tumor size, tumor side, previous abdominal surgery, resection method and pathology type.

Statistical analysis
All the continuous data was expressed as mean ± standard deviation; discontinuous data was presented as percentage. Statistical analyses were performed using SPSS version 20.0 (SPSS Inc, Chicago, IL). Two independent sample t tests were used in the continuous variables, and the Chi-square tests were used in the discontinuous variables. Curve estimations were used to explore the correlation between diameter and other potential factors. The estimating model included linear, logarithmic, inverse, quadratic, cubic, compound, power, s curve, growth curve and exponential. P < 0.05 was regarded as the difference between significant groups.

Results
Basic characteristics
Sixty seven adrenalectomies were performed between
January 2011 and June 2015 at Zigong No.4 people’s hospital. Of these, 41 patients underwent LRA and 26 patients underwent OA. The mean age for all cases was 42.3±13.9 years and there were 39 (58.2%) males. The mean tumor size was 6.9±2.7 cm. Tumor localization and peritoneal invasion of each patient was previously evaluated by CT scan. There were 40 cases (59.7%) of left localization of tumor, and tumors in two cases (2.9%) were bilateral. Of the patients, 49 cases (73.1%) had the diagnosis of aldosterone-producing adenoma or adrenocortical hyperplasia, 7 cases (10.4%) had the diagnosis of pheochromocytoma. There were 3 cases (4.5%) of hematoma and adrenal cyst. In the case series, there was 1 adrenocortical carcinoma (ACC) of LRA and 2 ACC of OA. Because this type of adrenal tumor is considered a malignant mass, the ACC in LRA group was converted to HARA. The remaining two cases were respectively diagnosed as adrenal medullary hyperplasia and myelolipoma. Total adrenalectomies were performed in 41 cases (61.2%). There were no significant differences between the two groups in all the basic characteristics (P > 0.05). Table 1 depicts the difference of basic characteristics between groups.

Operative terms comparison
Table 2 lists details on operative variables of two groups. The mean operation time for LRA was 98.7±32.3 min, while this time in OA group was 152.7±72.3 min, the difference between the groups was significant (P= 0.001). Estimated blood loss (EBL) was 31.9±20.0 ml for LRA and 590.0±1181.1 ml for OA (P= 0.03). There was no complication in LRA group, while one patient in OA group had high fever after operation, and the temperature dropped to normal after use of antibiotics. The difference of complication was not significant (P= NS). The post-operative hospitalization in LRA was 7.4±2.8 days, and this was shorter than 9.8±2.7 days in OA group (P= 0.00). The time to first oral intake and ambulation for LRA was shorter than OA (first oral intake, 1.9±0.8 days vs 3.1±1.3 days, P= 0.00; time to ambulation, 2.6±1.4 days vs 4.2±1.6 days, P= 0.00). While the difference between groups were not significant in terms of ICU conversion (3/41 vs 4/26, P= NS) and duration of drain (3.9±2.2 days vs 4.7±1.9 days, P= NS).

<table>
<thead>
<tr>
<th>Table 1. Basic characteristics comparison between groups.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of patients</strong></td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
</tr>
<tr>
<td>Tumor size (cm)</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Localization</td>
</tr>
<tr>
<td>Left</td>
</tr>
<tr>
<td>Right</td>
</tr>
<tr>
<td>Bilateral</td>
</tr>
<tr>
<td>Previous abdominal surgery</td>
</tr>
<tr>
<td>Resection</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Partial</td>
</tr>
<tr>
<td>Pathology</td>
</tr>
<tr>
<td>Adrenocortical hyperplasia</td>
</tr>
<tr>
<td>Aldosterone-producing adenoma</td>
</tr>
<tr>
<td>Adrenal medullary hyperplasia</td>
</tr>
<tr>
<td>Adrenal myelolipoma</td>
</tr>
<tr>
<td>Adrenocortical carcinoma</td>
</tr>
<tr>
<td>Adrenal cyst</td>
</tr>
<tr>
<td>Hematoma</td>
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<tr>
<td>Pheochromocytoma</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Operative and postoperative outcomes comparison between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of patients</strong></td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>Operation time</td>
</tr>
<tr>
<td>Estimated blood loss</td>
</tr>
<tr>
<td>Hospitalization</td>
</tr>
<tr>
<td>Duration of drain</td>
</tr>
<tr>
<td>First oral intake</td>
</tr>
<tr>
<td>Time to ambulation</td>
</tr>
</tbody>
</table>

BMI, body mass index; LRA, retroperitoneoscopic adrenalectomy; OA, open adrenalectomy

ICU, intensive care unit; LRA, retroperitoneoscopic adrenalectomy; OA, open adrenalectomy
Correlation of diameter and operation variables
We performed the curve estimation to investigate the correlation of diameter and each operation variable. The result presented that tumor diameter was positively correlation with estimated blood loss (R= 0.68, P< 0.01), operation time (R=0.46, P=0.00) and duration of drain (R= 0.26, P= 0.04) in the estimating model. However, the tumor diameter was not associated with the hospitalization, time to ambulation and first oral intake (P>0.05). Table 3 summarizes the adjusted correlation index and its P value of entire estimation.

Table 3. Correlation between diameter and each operation variable

<table>
<thead>
<tr>
<th>Variable</th>
<th>(R^2)</th>
<th>R</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation time</td>
<td>0.21</td>
<td>0.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Estimated blood loss</td>
<td>0.46</td>
<td>0.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>0.01</td>
<td>0.12</td>
<td>0.41</td>
</tr>
<tr>
<td>Duration of drain</td>
<td>0.07</td>
<td>0.26</td>
<td>0.04</td>
</tr>
<tr>
<td>Fist oral intake</td>
<td>0.01</td>
<td>0.11</td>
<td>0.25</td>
</tr>
<tr>
<td>Time to ambulation</td>
<td>0.01</td>
<td>0.09</td>
<td>0.19</td>
</tr>
</tbody>
</table>

\(R^2\), adjusted coefficient of determination; R, adjusted correlation index

Studies on laparoscopic adrenalectomy versus open procedure
We also retrieved studies that focused on the laparoscopic adrenalectomy (LA) for large adrenal tumors. A total of 9 studies\textsuperscript{15-24} mentioned the comparison on LA and OA, and two studies\textsuperscript{25,26} mentioned different diameter of adrenal tumor in LA. There exists controversy on the advantages of laparoscopy, as shown in the summarized information of related studies listed in Table 4.

Table 4 Studies on the laparoscopic adrenalectomy for tumors larger than 5cm

<table>
<thead>
<tr>
<th>First Author</th>
<th>Year</th>
<th>Origin country</th>
<th>Patients(^*)</th>
<th>Compare outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brix</td>
<td>2010</td>
<td>Germany</td>
<td>OA 117</td>
<td>Lap is not inferior to OA for adrenal tumor (\leq 10) cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lap 35</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OA 25</td>
<td>No differences in terms of survival time were noted</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lap 18</td>
<td></td>
</tr>
<tr>
<td>Poripiglia</td>
<td>2010</td>
<td>Italy</td>
<td>OA 71</td>
<td>Lap is inferior to OA for adrenal tumor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lap 17</td>
<td></td>
</tr>
<tr>
<td>Miller</td>
<td>2010</td>
<td>USA</td>
<td>OA 26</td>
<td>Lap is inferior to OA for adrenal tumor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lap 18</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OA 133</td>
<td>Lap is inferior to OA for adrenal tumor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lap (\geq 8)cm</td>
<td></td>
</tr>
<tr>
<td>Gonzales</td>
<td>2005</td>
<td>USA</td>
<td>Lap 6</td>
<td>Lap is inferior to OA for adrenal tumor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lap (\geq 8)cm</td>
<td></td>
</tr>
<tr>
<td>Bozkurt</td>
<td>2015</td>
<td>Turkey</td>
<td>Lap (&lt; 8)cm</td>
<td>LA is safe and effective for adrenal tumor (&lt; 15) cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lap (&lt; 5)cm</td>
<td>(\geq 5)cm prolonged hospital stay (HR 0.67; 95 % CI 0.47-0.97)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lap (\geq 8)cm</td>
<td>(\geq 8)cm prolonged operative time (HR 0.47; 95 % CI 0.24-0.94)</td>
</tr>
<tr>
<td>Feo</td>
<td>2015</td>
<td>Italy</td>
<td>Lap (&lt; 8)cm</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lap (&lt; 5)cm</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Lap (\geq 8)cm</td>
<td></td>
</tr>
<tr>
<td>Donatini</td>
<td>2014</td>
<td>France</td>
<td>OA 21</td>
<td>Lap is not inferior to OA for adrenal tumor (\leq 10) cm</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Lap 13</td>
<td></td>
</tr>
<tr>
<td>Cooper</td>
<td>2013</td>
<td>USA</td>
<td>OA 46</td>
<td>Lap is inferior to OA for adrenal tumor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lap 46</td>
<td></td>
</tr>
<tr>
<td>Fossa</td>
<td>2013</td>
<td>Norway</td>
<td>OA 15</td>
<td>Lap is inferior to OA in short-term and similar with OA in long-term for adrenal tumor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lap 17</td>
<td></td>
</tr>
<tr>
<td>Lombardi</td>
<td>2012</td>
<td>Italy</td>
<td>OA 126</td>
<td>Lap is not inferior to OA for adrenal tumor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lap 13</td>
<td></td>
</tr>
<tr>
<td>Levouilleux</td>
<td>2010</td>
<td>France</td>
<td>OA 58</td>
<td>Lap is inferior to OA for adrenal tumor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lap 6</td>
<td></td>
</tr>
</tbody>
</table>

\(* OA, Open adrenalectomy; Lap, Laparoscopic adrenalectomy

Discussion
Adrenal surgery has been a high-risk operation in urology for a long time. Due to the special location of the adrenals, even when dealing with a small diameter adrenal tumor, it needs a large incision and high position to carry out the operation\textsuperscript{27}. This method has not only caused great trauma to patients, but also significantly improves the proportion of pleural lesions and surgical complica-
tions. Most important adrenal vasculature can only be liga-
ted through blind separation and hand feeling for the rea-
son that most adrenals could show difficulties; this in-
creased the probability of tissue injury and hemorrhage.28
Laparoscopic adrenal surgery could be a finer and conve-
nient operation. It can clearly separate the important ves-
sels under a direct vision. This technique can significantly
decrease the post-operative complications.29

There are many methods of minimally invasive surger-
ies in the management of adrenal tumors. According to
the different surgical approaches, they can be divided
into transperitoneal and retroperitoneal laparoscopy ad-
renalectomy (RLA).30 Advantages and disadvantages have
been reported on the transperitoneal and retroperitoneal
adrenalectomy. The transperitoneal approach can ben-
efit from more visibility and larger working space, as well
as most familiar anatomy for surgeons. Previous opinion
shows that TLA is better than RLA in the treatment of
large adrenal tumors (> 5 cm). However, in TLA, there is
need to mobilize intra-abdominal structures and organs,
which has a high risk for organ or vascular injury. The
complications of TLA also include prolonged ileus and
the risk of adhesion formation. In the treatment of pa-
tients who received previous abdominal surgery, the TLA
is especially difficult to perform. While RLA owns obvi-
ous advantages, as it has a more direct route and doesnot
interfere with the intra-abdominal organs. In our previous
research, we identified that the operative time in RLA is
shorter than TLA.30 With the development of minimally
invasive surgery, scholars constantly show that the large
adrenal tumor can also benefit from RLA approach.

In the RLA, we can also divide it in lateral, posterior and
anterior approach. Since Zhang et al.31 made the lateral
retroperitontoscopy adrenalectomy (LRA) promotion
and standardization, it has been the most common meth-
ood in dealing with adrenal tumor in China. In our ex-
perience, even though the retroperitoneal approach is diffi-
cult, it is beneficial in the post-operative recovery. Since
the improvement of laparoscopic instruments and pro-
iciency of operation skill, the tumor diameter may not
be the major restricting factor.32 While, there were dis-
crepantry opinions on the application of laparoscope in the
management of large (> 5 cm) adrenal tumor.33,34 The aim
of the present study was to compare the results of LRA
and OA in the management of large adrenal tumors (> 5 cm).
The results revealed that the LRA was superior to
OA in terms of operation time, intraoperative blood loss,
post-operative hospitalization, complication, first oral in-
take and time to ambulation. There were three patients in
LRA group and 4 patients in OA group who converted to
ICU. Among these patients, five cases were pheochromocy-
toma (PHEO), with unstable blood pressure. Abnormal
blood vessels and huge volume can always be found in
PHEO cases. Additionally, catecholamines would be overly secreted during the tumor disturbance.35 Both
these features could lead to sharp fluctuations in blood
pressure and heart rate, and increase the risk of bleeding.
The complication of LRA was around 11.5%, and includ-
ed adrenal cataclastic, peritoneal injury, vena cava and re-
nal vein injury.36 In addition, the hypercapnia and pneu-
moderm which are caused by high pressure of CO2 or the
shallowly insertion of Trocar can also happen.37 Usually,
the CO2 insufflation pressure was proper when between
12 and 15 cmH2O according to our experience. Studies
showed that these complications were mainly related with
learning curve and different surgeons.38,39

Bleeding in LRA will inevitably be less with a small inci-
sion and slightly tissue injury. Our experience suggested
that we can inject approximately 350 ml normal saline
into a self-made gasbag to expand the potential peritoneal
cavity. Then followed by 3 minutes’ compression in order
to prevent the bleeding caused by small blood vessel rup-
ture. In addition, ultrasonic knife could be widely used in
the solidification of small blood vessels during the sepa-
ration of renal fascia and adipose capsule. However, open
surgery hemostasis would be chosen without any hesita-
tion when the operating vision was influenced by adrenal
cataclastic or unmanageable vascular injury.40

Limitations
There were certain limitations of LRA that we need to
take into consideration. The restricted potential cavity
limited the diameter of removable tumor. The interac-
tion of surgical instruments could also obviously affect
the ease of operation. Many scholars have reported that
the retroperitoneal laparoscope could just be used in the
small- to medium-sized benign adrenal tumor.41 How-
ever, the evidence from our present study has removed
this restriction. Moreover, the normal anatomic marks of
peritoneal cavity would be disturbed by the use of gasbag,
which was usually used to expand the peritoneal cavity.
This may also enhance the difficulty of operation. More
importantly, the effect of gas bag extrusion could also
make the tumor over-secret catecholamines in PHEO cases, therefore the pre-operative blood pressure and sphygmos control are very important.

In summary, LRA provides a new way of minimally invasive surgery for the surgical treatment of the adrenal disease. It was superior to open surgery in management of large adrenal tumors, in terms of operation time, intraoperative blood loss and post-operative recovery. Our result has strengthened the opinion that there is availability of LRA for adrenal tumor greater than 5 centimeters. Uro-surgeons or endocrinology surgeons could take LRA into consideration when they deal with large adrenal tumors.

**Conflict of interest**

None.

**Reference**


