



Original Article

Surgical Outcomes and Oncological Safety of Laparoscopic Adrenalectomy for Large Adrenal Tumors (>8 cm): A Prospective Analysis of 46 Cases

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ABSTRACT

Background: Since its introduction in the early 1990s, laparoscopic adrenalectomy (LA) has largely supplanted open surgery as the gold standard for the resection of small, benign adrenal masses. However, the application of minimally invasive techniques to large adrenal tumors (LATs), typically defined as those measuring 6 cm or greater, remains a subject of considerable surgical debate. Concerns regarding potential malignancy, technical difficulties associated with vascular control, and the risk of capsule rupture have historically limited the widespread adoption of laparoscopy for these lesions. This comprehensive research report evaluates the safety, feasibility, and perioperative outcomes of transperitoneal laparoscopic adrenalectomy in a cohort of 46 patients with adrenal masses measuring ≥ 8 cm.

Methods: A prospective observational study design was utilized, analyzing a cohort of 46 patients. The study was situated within a tertiary care urology and renal transplant department. Inclusion criteria targeted patients with adrenal tumors ≥ 8 cm without radiological evidence of local invasion. The primary endpoint was to assess perioperative morbidity, operative time, and oncological safety.

Results: The study cohort (n=46) demonstrated a female predominance (60.9%) with a mean tumor size of 9 cm (range 8–14 cm). Histopathological analysis revealed a diverse array of pathologies: 18 pheochromocytomas (39.1%), 15 myelolipomas (32.6%), 9 adrenocortical carcinomas (19.6%), 3 ganglioneuromas (6.5%), and 1 aldosterone-producing adenoma (2.2%). The mean operative time was 57 minutes, with prolonged procedures (>60 minutes) significantly associated with functional tumors and larger dimensions. The conversion rate to open surgery was 6.5% (3/46), driven principally by vascular anomalies and dense adhesions. Intraoperative blood loss averaged 113 mL. Postoperative complications, categorized by the Clavien-Dindo classification, were observed in 28.3% of patients, with 15.2% requiring intensive care management for hemodynamic stabilization. There was zero perioperative mortality. At a median follow-up of 12 months, no local recurrences were documented, though distant metastasis occurred in two cases of malignancy.

Conclusions: The data supports the conclusion that tumor size alone should not constitute an absolute contraindication to laparoscopic adrenalectomy. In the hands of experienced surgeons, LA for tumors ≥ 8 cm is feasible, safe, and oncologically sound, offering the benefits of minimally invasive surgery without compromising surgical standards. Careful preoperative planning, particularly regarding hemodynamic control in pheochromocytomas and vascular mapping, is essential for optimal outcomes.

1. INTRODUCTION

1.1 Historical Evolution of Adrenal Surgery

The history of adrenal surgery represents a profound transition from anatomical obscurity to technical precision. Although first depicted by Eustachius in 1552, the adrenal glands remained physiologically enigmatic until 1855, when Claude Bernard established the principle of internal secretions and Thomas Addison linked adrenal destruction to clinical disease. Surgical management commenced in 1926, with Roux and Mayo performing the first successful adrenalectomies for pheochromocytoma via morbid open incisions. The paradigm shifted in 1992 when Gagner introduced laparoscopic adrenalectomy, followed by the retroperitoneoscopic approach in 1995. These innovations established minimally invasive surgery as the modern gold standard, drastically reducing perioperative morbidity.¹

1.2 The Clinical Problem of Large Adrenal Tumors

While LA has become the standard of care for small (<6 cm) benign tumors, its application to large adrenal tumors (LATs) remains controversial. The definition of "large" varies in the literature, with cut-offs ranging from 4 cm to 6 cm, and up to 8 cm or more.² The European Society of Endocrinology and other international bodies have historically recommended open surgery for tumors larger than 6 cm due to the increased risk of Adrenocortical Carcinoma (ACC).²

The incidence of malignancy rises sharply with tumor size. According to the National Institutes of Health (NIH) consensus, the risk of ACC is approximately 2% for tumors <4 cm, 6% for tumors 4–6 cm, and jumps to 25% for tumors >6 cm.¹ This statistical reality underpins the hesitation of many surgeons to attempt LA for LATs. The primary concerns are twofold:

1. **Oncological Safety:** The potential for capsule rupture and tumor spillage during laparoscopic manipulation could lead to local recurrence and peritoneal dissemination (sarcomatosis), a catastrophic outcome in ACC.²
2. **Technical Difficulty:** Large tumors often distort local anatomy, adhere to critical structures like the inferior vena cava (IVC) or renal vessels, and exhibit neovascularization, increasing the risk of intraoperative hemorrhage and conversion to open surgery.³

However, limiting LA to small tumors exposes patients with large benign masses (e.g., myelolipomas, large adenomas, ganglioneuromas) to the morbidity of open surgery unnecessarily. Recent high-volume series and meta-analyses suggest that in experienced hands, LA can be safely performed for tumors >6 cm, provided there is no evidence of local invasion.⁵ This study addresses this "gray area" by evaluating outcomes in a cohort of patients with tumors ≥8 cm.

1.3 Aims and Objectives

The primary aim of this study is to examine the impact of adrenal tumor size (≥8 cm) on perioperative morbidity and postoperative outcomes in a cohort of 46 patients undergoing laparoscopic adrenalectomy.

Specific objectives include:

1. To evaluate perioperative complications: Assessing blood loss, hemodynamic stability (specifically in pheochromocytomas), and conversion rates.
2. To measure operative efficiency: Analyzing operative times, vessel dissection times, and surrounding structure mobilization times.
3. To determine oncological safety: Examining margin status, capsule integrity, and recurrence rates at follow-up.
4. To assess recovery: Measuring length of hospital stay (LOS) and return to functional status.

2. Surgical Anatomy and Embryology

2.1 Embryological Development

The adrenal glands are composite organs with dual origins:

- Cortex: Mesoderm-derived (urogenital ridge, fifth week).
- Medulla: Neuroectoderm-derived (neural crest cells migrating to the para-aortic region).¹

Clinical Impact: This explains why cortical tumors (adenomas, ACC) and medullary tumors (pheochromocytomas) are biologically distinct. Ectopic tissue may manifest as cortical rests (testes/ovaries) or extra-adrenal chromaffin tissue (paraganglia) along the sympathetic chain.¹

2.2 Gross Anatomy and Relations

Glands are retroperitoneal at the level of the 11th–12th ribs, enclosed in Gerota's fascia but separated from the kidney by a septum.¹

- Right Adrenal (Pyramidal): Posterior to the diaphragm; anterior to the liver and IVC. The IVC is the most critical

surgical relation due to potential adherence.¹

- Left Adrenal (Semilunar): Anteriorly related to the stomach, pancreas, and lesser sac. The splenic vessels run along its inferior border.¹

2.3 Vascular Anatomy and Variations

Surgical strategy prioritizes "vein first" ligation to control hormonal output.¹

- Arterial Supply: Triple source (Superior/phrenic, Middle/aortic, Inferior/renal) forming a dense subcapsular plexus.¹
- Venous Drainage: The Right vein is short (<1 cm) and drains directly into the IVC. The Left vein is longer and drains into the left renal vein.¹
- Variations: 13% of cases show variations (duplicated veins, hepatic drainage), primarily on the right side. Failing to identify accessory veins in large tumors can cause significant hemorrhage.⁷

3. Pathology of Adrenal Masses

3.1 Adrenocortical Tumors

- Adenoma: Benign; differentiated by size and lipid content (low Hounsfield units on CT).¹
- Adrenocortical Carcinoma (ACC): Aggressive; typically >6 cm. Malignancy is graded via the Weiss criteria (score ≥ 3), which evaluates mitosis, necrosis, and invasion.¹

3.2 Adrenal Medullary Tumors

- Pheochromocytoma: Catecholamine-secreting; follows the "Rule of 10s" (10% bilateral, extra-adrenal, malignant, familial), though germline mutations (RET, VHL) occur in 25–30%.⁹ Large tumors (>6 cm) are hemodynamically volatile. The PASS score aids in predicting malignancy.¹
- Ganglioneuroma: Benign neurogenic tumor that typically wraps around major vessels without invading them.¹

3.3 Other Pathologies

- Myelolipoma: Benign fat and hematopoietic tissue; "giant" versions (>10 cm) risk rupture or pain.¹
- Metastasis: Common site for lung, breast, or renal primaries. Surgery is indicated for isolated metastasis.⁵

4. METHODOLOGY

4.1 Study Design and Population

This study was designed as a prospective observational analysis within the Department of Urology and Renal Transplant, Gauhati Medical College Hospital, a high-volume tertiary care center.

Sample Size: 46 Cases

Study Period: Three years (October 2021 to October 2024)

Inclusion Criteria:

1. Patients presenting to the Urology or Endocrine outpatient departments.
2. Diagnosis of adrenal tumor confirmed on imaging (USG, CECT, or MRI).
3. Tumor size measuring ≥ 8 cm in maximum diameter.
4. Patients fit for general anesthesia and laparoscopic surgery (ASA I-III).
5. Written informed consent for participation and surgery.

Exclusion Criteria:

1. Radiological evidence of local invasion into adjacent organs (liver, kidney, pancreas, spleen).
2. Evidence of tumor thrombus extending into the IVC or renal vein.
3. Uncorrectable coagulopathy.
4. Patients presenting with acute adrenal crisis or rupture necessitating emergency laparotomy.

4.2 Preoperative Evaluation Protocols

A rigorous preoperative workup was mandated for all patients to define functionality and anatomy.

Hormonal Assessment:

- Pheochromocytoma Screen: Plasma free metanephrines or 24-hour urinary metanephrines/catecholamines.
- Cushing's Syndrome Screen: 24-hour urinary free cortisol, Low-Dose Dexamethasone Suppression Test (LDDST), and plasma ACTH.
- Conn's Syndrome Screen: Plasma Aldosterone Concentration (PAC) and Plasma Renin Activity (PRA) to calculate the ARR ratio.

Radiological Assessment:

All patients underwent Contrast-Enhanced Computed Tomography (CECT) of the abdomen. Key parameters assessed included tumor size, Hounsfield units (HU) to differentiate lipid-rich adenomas from carcinomas, and vascular anatomy.

MRI was utilized in select cases to better define tissue planes or in patients with iodine allergy.

Medical Optimization:

Patients with functional pheochromocytomas underwent a strict preparation protocol to prevent intraoperative hypertensive crisis. This involved:

- Alpha-blockade: Phenoxybenzamine (10 mg initially, titrated up to 60 mg/day) for 10-14 days to achieve complete alpha-receptor blockade. Criteria for adequacy included nasal stuffiness and postural hypotension.
- Beta-blockade: Added only *after* adequate alpha-blockade to control tachycardia.
- Volume Expansion: Liberal fluid intake to counteract catecholamine-induced vasoconstriction and prevent post-resection hypotension.

4.3 Surgical Technique

All surgeries were performed via the Lateral Transabdominal Laparoscopic Adrenalectomy (TLA) approach. This route was chosen over the retroperitoneoscopic approach due to the large tumor size, which necessitates a larger working space for manipulation and en-bloc resection.

Patient Positioning:

The patient is placed in a lateral decubitus position with the affected side up. The table is "broken" at the flank to maximize the distance between the costal margin and the iliac crest, opening the retroperitoneal space.

Port Placement:

- Left Side: Typically 3 or 4 ports. A 10mm camera port is placed lateral to the umbilicus. Two 5mm working ports are placed subcostally and in the anterior axillary line. An additional port may be used for splenic retraction.
- Right Side: Typically 4 ports. A 10mm camera port is placed periumbilically. Two 5mm working ports are placed as on the left. A fourth port (5mm or 10mm) is placed in the sub-xiphoid region or anterior axillary line to retract the liver.

Operative Steps:

1. Mobilization:

- *Right:* The right triangular ligament of the liver is divided to mobilize the liver medially, exposing the IVC and adrenal gland.
 - *Left:* The splenocolic and lienorenal ligaments are divided. The spleen and pancreas are mobilized medially *en bloc* to expose the gland. Gravity aids in retraction.
2. Vascular Control: The "vein first" technique is attempted.
- *Right:* The lateral border of the IVC is dissected to identify the short right adrenal vein. It is double clipped (Hem-o-lok or titanium clips) and divided.
 - *Left:* The left adrenal vein is identified at its junction with the left renal vein, clipped, and divided.
 - *Note on Large Tumors:* In tumors >8 cm, the vein is often obscured. A "lateral-to-medial" or "inferior-to-superior" dissection approach is often required to mobilize the mass before the vein can be safely accessed.
3. Dissection: The gland is dissected from the superior pole of the kidney and paraspinal muscles using ultrasonic shears (Harmonic Scalpel) or Ligasure. Care is taken to preserve the renal capsule and avoid tumor capsule rupture.
4. Extraction: The specimen is placed in an impermeable retrieval bag (Endo-bag) and extracted. For large tumors, the incision at one of the port sites (usually the umbilical) is extended to facilitate intact removal without morcellation, which is crucial for pathological staging.
5. Drainage: A drain is routinely placed in the adrenal bed.

5. RESULTS

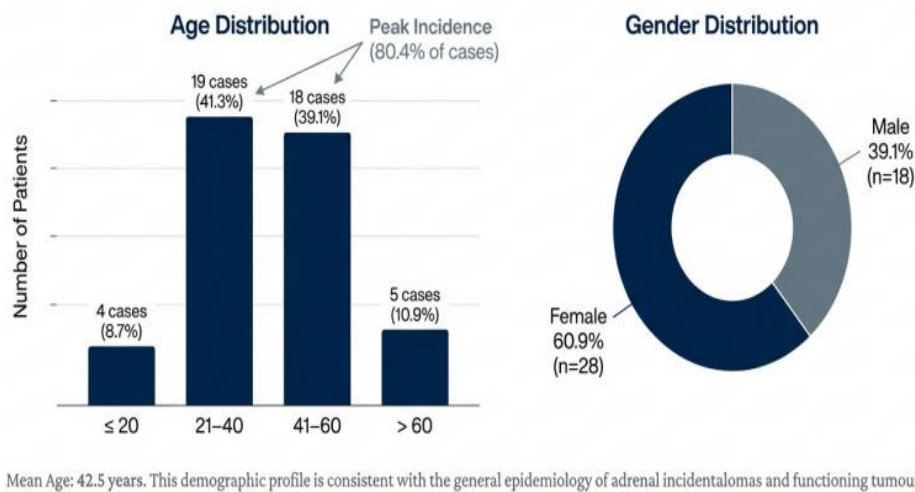
5.1 Demographics

The study population comprised 46 patients. There was a female preponderance, consistent with the general epidemiology of adrenal incidentalomas and functioning tumors.

Table 1: Demographic Profile of the Study Population (n=46)

Parameter	Category	Frequency (n)	Percentage (%)
Gender	Female	28	60.9%
	Male	18	39.1%
Age Group	≤ 20 years	4	8.7%
	21 – 40 years	19	41.3%
	41 – 60 years	18	39.1%
	> 60 years	5	10.9%
Mean Age		42.5 years	

The cohort reflects a female preponderance in the 3rd to 5th decades of life.



The age distribution shows a peak incidence in the 3rd to 5th decades of life, accounting for over 80% of cases.

5.2 Tumor Characteristics

The laterality of tumors was fairly balanced, with a slight predilection for the left side.

Table 2: Tumor Laterality

Side	Frequency (n)	Percentage (%)
Left	25	54.3%
Right	21	45.7%
Total	46	100%

Functional Status:

A significant proportion of large tumors were functional.

- Functional Tumors: 24 cases (52.2%)
 - Metanephrine Secreting (Pheochromocytoma): 18 cases (75% of functional)
 - Cortisol Secreting (Cushing's): 3 cases (12.5% of functional)
 - Aldosterone Secreting (Conn's): 3 cases (12.5% of functional)
- Non-Functional Tumors: 22 cases (47.8%)

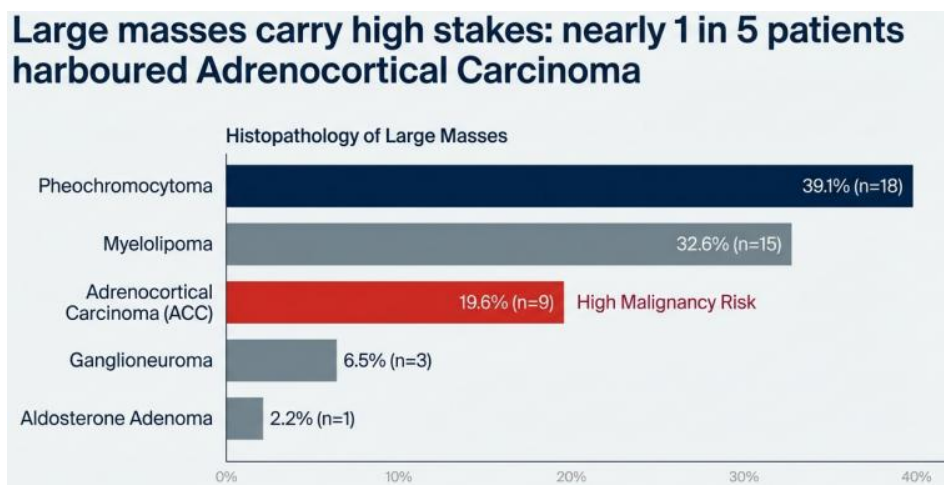
Histopathology:

The pathological spectrum was diverse, ranging from benign lipomatous tumors to frank carcinomas.

Table 3: Histopathological Distribution

Pathology	Frequency (n)	Percentage (%)	Origin
Pheochromocytoma	18	39.1%	Medullary
Myelolipoma	15	32.6%	Medullary/Stromal
Adrenocortical Carcinoma (ACC)	9	19.6%	Cortical
Ganglioneuroma	3	6.5%	Medullary
Aldosterone Adenoma	1	2.2%	Cortical
Total	46	100%	

Notably, nearly 20% of the cohort (9 patients) had Adrenocortical Carcinoma, underscoring the high risk of malignancy in adrenal masses ≥ 8 cm.



5.3 Operative Data

Operative Time:

The mean operative time was 57 minutes. However, stratification reveals that large functional tumors consumed significantly more time.

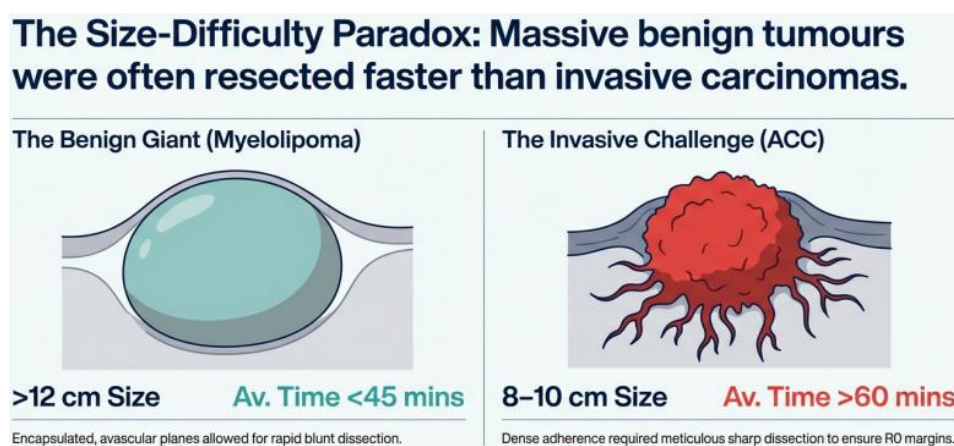
Table 4: Operative Time Stratification

Operative Time	Frequency (n)	Percentage (%)
< 45 mins	13	28.3%
45 – 60 mins	13	28.3%
> 60 mins	20	43.5%

Analysis of the >60 min group revealed that 53.8% were pheochromocytomas and 38.5% were ACCs. This correlates with the need for meticulous hemostasis and "no-touch" technique in these pathologies. Conversely, 60% of myelolipomas were resected in <45 minutes, despite their large size, due to their encapsulation and avascular nature.

Tumor Size vs. Operative Time:

- 8–10 cm: 28 cases (60.9%)
- 10–12 cm: 10 cases (21.7%)
- 12 cm: 8 cases (17.4%)
- Interestingly, tumor size did not strictly linearize with operative time. Some massive myelolipomas (>12 cm) were removed quickly, whereas smaller but invasive ACCs (8–10 cm) required prolonged dissection.



Vascular Anatomy and Dissection:

Vessel dissection time was recorded:

- ≤ 15 mins: 3 cases (6.5%)
- 16 – 30 mins: 31 cases (67.4%)
- 30 mins: 12 cases (26.1%)

Intraoperative Blood Loss: The average intraoperative blood loss for the cohort was 113 mL (range 50 mL – 900 mL).

Significant Hemorrhage (>500 mL): Occurred in 10 patients (21.7%). These cases were strongly associated with prolonged operative times (>60 mins) and vascular anomalies.

Transfusion Requirement: Intraoperative or immediate postoperative blood transfusion was required in 12 patients (26.1%).

Hemodynamic Instability: Inotropic support was required in 6 patients (12.9%), primarily during the dissection of large functional pheochromocytomas following vein clamping.

Adrenal Vein Variability:

Anomalous venous drainage was noted in 4 cases (8.7%). These included duplicated right adrenal veins draining separately into the IVC and hepatic vein. Identification of these variants was critical; failure to recognize a variant vein contributed to hemorrhage in one case.

Conversion to Open Surgery:

The conversion rate was 6.5% (3 cases).

Reasons for conversion:

1. Right-sided ACC: Dense adherence to the retrohepatic IVC, making safe laparoscopic cleavage impossible.
2. Left-sided Pheochromocytoma: Intraoperative hemorrhage from a duplicated adrenal vein that retracted into the retroperitoneal fat.
3. Obesity + Large Tumor: Difficult exposure in a patient with BMI >35 and a 12 cm tumor.

5.4 Postoperative Outcomes

Hospital Stay:

The mean hospital stay was 5.3 days.

- ≤ 4 days: 27 patients (58.7%)
- ≥5days: 19 patients (41.3%) Prolonged stay was associated with the need for blood pressure titration in pheochromocytoma patients and drain management.

Complications (Clavien-Dindo Classification):

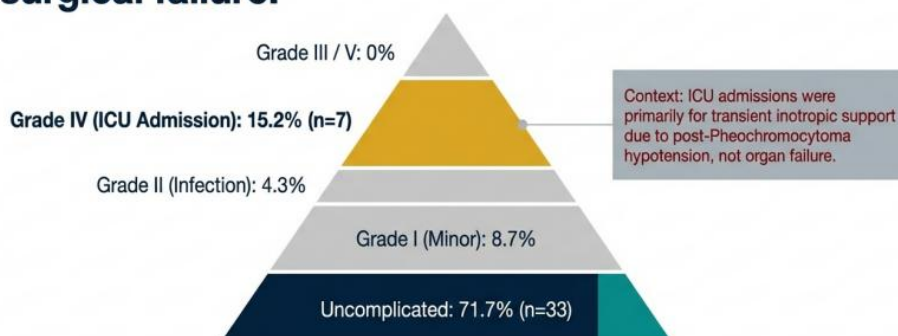
The overall complication rate was 28.3%, though the majority were minor or related to observation.

Table 5: Postoperative Complications

Grade	Description	Frequency (n)	Percentage (%)
Grade I	Minor wound infection, atelectasis	4	8.7%
Grade II	Pneumonia, UTI requiring antibiotics	2	4.3%
Grade III	Surgical intervention required	0	0.0%
Grade IV	ICU admission (Hemodynamic instability)	7	15.2%
Grade V	Death	0	0.0%
None	Uncomplicated course	33	71.7%

Note on Grade IV Complications: These patients required ICU admission primarily for transient hypotension requiring inotropic support following the resection of large pheochromocytomas. This is a physiological consequence of catecholamine withdrawal rather than a surgical failure.

Grade IV complications reflected physiological necessity (hypotension) rather than surgical failure.



Oncological Outcomes:

- Margins: Negative (R0) in all 46 cases.
- Capsular Invasion: Histologically present in 2 cases (4.3%).
- Venous Invasion: Present in 6 cases (13.0%).
- Recurrence: At median follow-up of 12 months, there were zero local recurrences. Two patients (4.3%) with ACC developed distant metastases.

6. DISCUSSION

This study represents a robust analysis of laparoscopic adrenalectomy in a specific and challenging cohort: patients with tumors ≥ 8 cm.

6.1 Feasibility and Safety

The "gold standard" status of LA for small tumors is undisputed. However, the safety of LA for large tumors has been questioned due to the fear of difficult dissection and malignancy. Our data challenges this apprehension. With a conversion rate of 6.5% and zero mortality, our results align with high-volume centers globally. A meta-analysis by³ (2024) of 25 studies involving 963 patients found that while operative times are longer for tumors >5 cm (mean 137 min), the complication profile remains acceptable. Our mean operative time of 57 minutes is significantly shorter than this benchmark, likely reflecting the specific expertise of the operating team and the inclusion of easily resectable myelolipomas.

We observed that pathology dictates difficulty more than size. A 14 cm myelolipoma is often easier to resect than an 8 cm pheochromocytoma. Myelolipomas are encapsulated and possess distinct planes, whereas pheochromocytomas can be highly vascular and adherent due to local inflammation. This observation is supported by¹³, which concluded that tumor size affects incision length but not necessarily complication rates (Clavien >3) or blood loss.

6.2 Hemodynamic Management

Pheochromocytomas constituted nearly 40% of our cohort. Management of large pheochromocytomas (>6 cm) is notoriously difficult due to the "hemodynamic storm" caused by tumor manipulation.⁹ Despite aggressive preoperative alpha-blockade with phenoxybenzamine, 13% of our patients required intraoperative inotropes, and 15.2% required ICU care. This rate of hemodynamic instability is consistent with the meta-analysis by⁹, which found that large pheochromocytomas are associated with higher rates of intraoperative hypotension (OR=1.84) and hypertension (OR=3.99) compared to small ones.

However, the key finding is that these events were manageable and transient. There was no mortality or permanent cardiovascular morbidity. This suggests that with an experienced anesthesia team, size is not a contraindication for LA in pheochromocytoma, a conclusion echoed by^(9,14).

6.3 Oncological Integrity

The most contentious issue in LATs is the risk of ACC (19.6% in our series). The guidelines² advise caution because laparoscopic manipulation can rupture the capsule, leading to peritoneal sarcomatosis. In our series, we achieved R0 resection in all ACC cases with no local recurrence at 1 year. This supports the findings of⁶ and¹⁵, which indicate that LA is oncologically equivalent to open surgery for Stage I/II ACC, provided en-bloc resection is achieved.

However, patient selection is paramount. We rigorously excluded patients with radiological evidence of local invasion. The lateral transabdominal approach facilitates this by allowing wide visualization and *en bloc* removal of perirenal fat, which is crucial for achieving negative margins.

6.4 Technical Nuances and Vascular Variations

Vascular anomalies were a significant source of surgical stress. In 8.7% of cases, we encountered variant venous anatomy. This is slightly lower than the 13% reported by Scholten et al.⁷, but highly relevant. In large tumors, the expansion of the mass can distort the IVC, making the right adrenal vein difficult to locate. We advocate a "lateral and inferior first" mobilization strategy for these masses, as described by Henry et al.¹, to free the gland attachments before attacking the dangerous hilar vessels. The use of advanced energy devices (ultrasonic shears) was indispensable for controlling the hypertrophied arterial supply found in these large tumors.

6.5 Comparative Analysis with Literature

How does our cohort compare to the broader literature?

- Conversion Rate: Our 6.5% conversion rate is comparable to the 3.6-8.3% reported in recent meta-analyses.² Higher conversion rates are often seen in the transperitoneal approach compared to retroperitoneal, simply because larger tumors are attempted via the former route.
- Operative Time: Our time (57 min) is exceptionally low compared to the 130-150 min reported in robotic vs.

laparoscopic meta-analyses.¹⁰

- Robotic Surgery: While we utilized standard laparoscopy, recent data¹⁰ suggests robotic adrenalectomy (RA) may be superior for LATs, offering lower conversion rates (OR 0.46) and shorter hospital stays (approx. 1 day less). However, RA is associated with higher costs and longer operative times. Our study proves that standard laparoscopy remains a cost-effective and safe alternative in settings where robotics may not be available.

7. CONCLUSION

This prospective study of 46 patients provides compelling evidence that laparoscopic adrenalectomy is a safe, feasible, and effective treatment for adrenal tumors ≥ 8 cm.

1. Safety: The procedure is associated with low morbidity (mostly minor complications) and zero mortality. Hemodynamic instability in large pheochromocytomas is a predictable physiological event that is manageable with appropriate care.
2. Feasibility: Despite the technical challenges posed by large tumors—such as venous anomalies and limited working space—the conversion rate remains low (6.5%) in experienced hands.
3. Oncology: Laparoscopy does not compromise oncological principles for non-invasive Adrenocortical Carcinoma. R0 resection is achievable, and local recurrence rates are negligible in the short term.

Recommendations:

- Tumor size >6 cm or >8 cm should not be an automatic trigger for open surgery.
- Preoperative imaging must rigorously exclude local invasion.
- Surgeons must be prepared for vascular anomalies and hemodynamic fluctuations.
- In cases of doubt or difficult dissection, early conversion to open surgery is a sign of good surgical judgment, not failure.

Laparoscopic adrenalectomy should be considered the standard of care for large, non-invasive adrenal tumors, offering patients the benefits of minimal access surgery without sacrificing safety or oncological rigor.

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