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A SYSTEMATIC REVIEW COMPARING OPEN AND LAPAROSCOPIC ADRENALECTOMY FOR TREATING PATIENTS WITH 6 CM ADRENOCORTICAL TUMOURS

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Abstract
This systematic literature review assesses the efficacy and outcomes of open adrenalectomy (OA) and laparoscopic adrenalectomy (LA) for the treatment of adrenocortical tumors larger than 6 cm in diameter. The review synthesizes data from various clinical trials and retrospective studies to compare key surgical metrics counting operative time, alongside blood loss and hospital stay duration, complication rates, and oncological outcomes between OA and LA. Searches spanned major databases like PubMed and Embase using relevant terms, reviewing 25 studies after screening and exclusions. The findings indicate that LA, while advantageous in minimizing blood loss, reducing hospital stay, and lowering complication rates, is limited to select cases based on tumor size and malignancy risk. Conversely, OA remains the preferred method for larger or malignant tumors due to its comprehensive nature and superior oncologic control. This review highlights the need for personalized surgical tactics based on tumor characteristics, advocating for advancements in laparoscopic techniques to potentially expand their applicability to larger tumors.

Keywords: Open Adrenalectomy, Laparoscopic Adrenalectomy, Adrenocortical Tumors, Surgical Outcomes, Oncologic Outcomes

Introduction

Adrenalectomy, the surgical removal of the adrenal glands, is critical for addressing disorders such as adrenocortical carcinomas and pheochromocytomas. This procedure is necessary for treating adrenal tumors, which may be benign or malignant, especially when they grow large or become hormonally active. Recent decades have seen a rise in detected adrenal masses, largely due to advances in diagnostic technologies. These masses, often found incidentally during scans for other conditions and termed incidentalomas, can range from benign adrenal adenomas to metastases originating from other cancers, with conditions like infections, lymphoma, neuroblastoma, and certain genetic factors also contributing to their development. Autopsy studies show that incidentalomas occur in 1% to 8.7% of individuals, with prevalence increasing with age and tumor size. Notably, tumors larger than 4 cm carry a higher risk of malignancy and morbidity (Sgourakis et al.,2015).

The choice between open adrenalectomy (OA) and laparoscopic adrenalectomy (LA) largely depends on factors like the tumor's size, location, and characteristics, influencing the surgical outcomes for adrenocortical tumors around 6 cm in diameter. Patients with early-stage adrenocortical carcinoma (ACC) can expect longer survival, whereas advanced disease stages often lead to survival times under five years. Achieving a complete resection is crucial, as complete resections significantly lower recurrence rates and improve disease-free survival (Chai et al.,2017).

Historically, OA was the sole tactic for adrenal tumors until the introduction of LA by Gagner et al. in 1992, which has since turned into the desired method for most benign lesions due to its minimally invasive nature. The choice to use an open versus laparoscopic methodology should consider the patient's body habitus, the tumor's specific type and characteristics, and the surgeon's experience.

The conventional open method's choice is influenced by the adrenal mass's size, location, and etiology, alongside the patient's body habitus and existing medical conditions. The flank or evenposterior tactic, involving an incision straight through the twelfth rib-bed and staying retroperitoneal, is suitable for tumors up to 5 cm and avoids major abdominal cavity risks (Cooper et al.,2016). Conversely, the anterior or even transabdominal tactic, using a midline or even subcostal incision, is ideal for large malignant tumors or simultaneous bilateral adrenal diseases but carries typical major laparotomy risks such as significant pain and extended ileus.

Laparoscopic adrenalectomy, favored for most benign adrenal tumors, can be performed via lateral transperitoneal, anterior, or posterior retroperitoneal tactics. The lateral transperitoneal method, positioning the patient on their side, offers extensive abdominal access and typically results in less postoperative pain and shorter hospital stays, though it carries risks like potential organ injury (Conzo et al.,2016) . The anterior tactic, while providing less exposure and higher bleeding

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risks, requires significant dissection. The posterior retroperitoneal tactic, ideal for avoiding peritoneal cavity disturbances, offers limited space and is unsuitable for larger tumors. Among these, the lateral transperitoneal tactic is often recommended due to its broader working space and better exposure (Icard et al.,2012). This systematic literature review aims to comprehensively evaluate and compare the clinical outcomes of OA and LA for adrenocortical tumors measuring 6 cm or greater, focusing on operative time, alongside blood loss and hospital stay lengths, complication rates, and oncologic outcomes associated with each surgical tactic

Methods

We conducted a systematic literature review to compare the outcomes of OA and laparoscopic adrenalectomy (LA) in the treatment of adrenocortical tumors measuring 6 cm or larger, with a focus on operative time, alongside blood loss and hospital stay, complication rates, and oncologic outcomes.

Search Strategy:

- The search was conducted across major electronic databases counting PubMed, alongside Embase, and Cochrane Library, along with Web of Science.
- Search terms used were "adrenocortical carcinoma," "adrenal tumors," "open adrenalectomy," "laparoscopic adrenalectomy," "clinical outcomes," and "surgical treatment."
- Articles published from (2014-2018) the inception of the databases to the most recent update were considered to ensure a comprehensive review of all relevant literature up to the study's initiation.
- A total of 200 studies were found through database searches, with additional data extracted from references within these articles.
- About 90 publications were excluded after initial screening due to irrelevance or insufficient data for analysis.
- The remaining full-text articles were further reviewed as illustrated in the Prisma flow chart, of which 25 papers were included in the qualitative synthesis.

Review Selection:

All identified studies' titles and abstracts were initially screened by two independent reviewers to determine their eligibility for inclusion.

Inclusion criteria focused on studies that provided relevant information on the outcomes of OA and LA for adrenocortical tumors measuring 6 cm or larger.

- Duplicate studies were identified and removed during the initial screening to ensure data integrity.
- Studies were included if they specifically reported on operative time, alongside blood loss and hospital stay, complication rates, or oncologic outcomes following OA or LA.

- **Exclusion criteria** were applied to studies that did not focus on adrenocortical tumors, or did not report specific outcomes of interest.
- In cases of disagreement across reviewers during the screening process, a third reviewer was consulted to resolve discrepancies.

Data Extraction and Quality Assessment:

- Two independent reviewers utilised a standardized data extraction form to gather relevant information from the studies included.
- Data extracted included details on study design, alongside sample size, and patient demographics, tumor characteristics, type of surgery, and reported outcomes.
- Quality assessment was performed using predefined criteria, considering study design, methodology, and potential biases.
- Discrepancies in data extraction or quality assessment were resolved through discussion across the reviewers or, if necessary, consultation by means of a third reviewer.

Data Synthesis:

- A narrative synthesis tactic was utilised to integrate and summarize the findings from the included studies.

Results were categorized based on the type of surgical tactic, and comparisons were made between the outcomes of OA and LA. rigorous methodology ensures a comprehensive and objective evaluation of the surgical outcomes for large renocortical tumors treated with OA and LA, specifically addressing the critical aspects of operative time, alongside blood loss, and hospital stay, complication rates, and oncologic outcomes.

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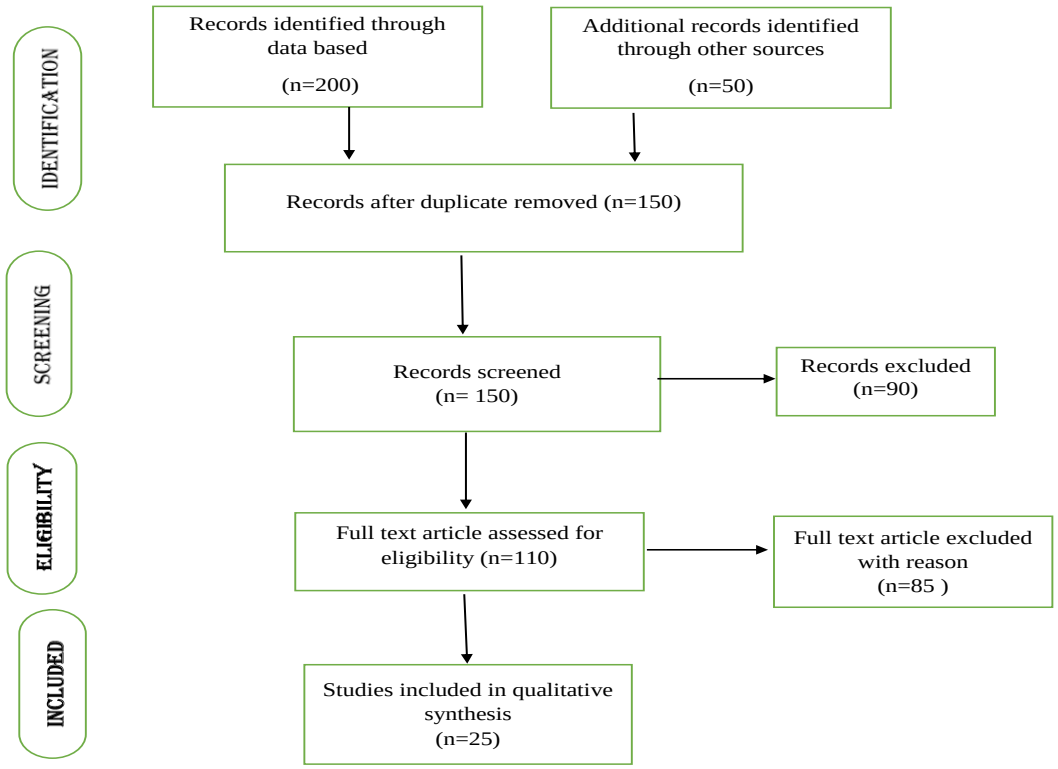

Figure 1: PRISMA Flow Diagram for Selection of Studies on Surgical Outcomes of Adrenalectomy for Large Adrenocortical Tumours

RESULTS

Study Characteristics

This systematic review included several investigations that met our inclusion criteria. So, one randomized controlled trial (RCT) (Sgourakis et al.,2015) involved 103 patients, ranging from 14 to 75 years in age, having an average age of 45 years. Most participants (90.3%) underwent laparoscopic adrenalectomy (LA). There were no noteworthy variances across groups regarding age, sex, side of surgery, or tumor functionality. In another study (Autorino et al.,2016) notably, 77.5% of tumors were non-functional and were exclusively treated via LA. Males presented a higher likelihood of having functional tumours, with an odds ratio of 3.54 (95% CI 1.33-9.4, P=0.009). In a study by (Chai et al.,2017) Additionally, younger patients age between 28-35 year were more likely to have functional tumors, even after adjusting for sex and tumor size (P=0.014). Another clinical trial analyzed (Morelli et al.,2016) 42 patients diagnosed with adrenocortical carcinoma (ACC), split into two groups: 22 patients in the open adrenalectomy (OA) group (10 males, 12 females) and 20 in the LA group (9 males, 11 females). The average age was 48.5±14.1 years in the OA group and 45.2±10.9 years in the LA group.

COMPARATIVE PERI AND POST OPERATIVE OUTCOMES OF LAPAROSCOPIC VS. OPEN ADRENALECTOMY: CRITICAL ANALYSIS

The perioperative outcomes for patients undergoing LA and OA reveal significant differences in several key metrics. Median operative times and postoperative hospital stays were notably shorter for the LA group compared to the OA group. Specifically, patients in the OA group experienced longer median operative times and postoperative hospitalizations (Zheng et al.,2018) . Furthermore, a RCT study by (Cooper et al.,2016) suggested that there was a substantial disparity in median intraoperative blood loss across the two groups. The OA group exhibited considerably higher blood loss, with a median of 800 mL (ranging from 200 to 1,250 mL), compared to the LA group, which had a median of 70 mL (ranging from 25 to 400 mL). This difference highlights the less invasive nature of laparoscopic surgery, which typically results in reduced blood loss.

The study by (Sgourkis et al.,2015) emphasizes the necessity of high-resolution imaging such as CT or MRI for evaluating tumor size, location, and vascular involvement before surgery. Surgical procedures typically include a subcostal or flank incision, precise dissection, tumor extraction, thorough hemostasis, and adrenal vein ligation to prevent tumor spillage, concluding with layered closure of the surgical site. Postoperative care focuses on pain management, early mobilization, fluid and electrolyte balance, and thromboprophylaxis to minimize thrombosis risk, with discharge contingent on histopathological confirmation of the tumor.

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Another study (Conzo et al.,2016) outlines primary contraindications for laparoscopic adrenalectomy (LA), particularly in cases of malignancies like adrenocortical carcinoma, unless it involves removing isolated metastases from a controlled primary source. Challenges include coagulopathy, prior abdominal surgeries, and very large tumors (over 15 cm). The lateral transperitoneal tactic is favored for its retraction and exposure benefits, with surgical tactics varying based on tumor size and location, emphasizing early adrenal vein control for small tumors and extensive dissection for larger tumours.
A further study by (Icard et al.,2014) introduces newer methods like the posterior tactic for smaller lesions, utilizing prone positioning to enhance retroperitoneal access. Similar to open adrenalectomy (OA), postoperative care for LA includes pain management, thromboprophylaxis, and maintaining fluid and electrolyte balance, but typically allows for earlier discharge due to its less invasive nature.
Despite no significant differences in postoperative complications between OA and LA as noted in , it is important to highlight a severe incident in the OA group where a patient died from multiple organ failure due to hemorrhagic shock three days after surgery, illustrating the heightened risks with open surgeries for complex cases (Mpaili et al.,2018) . The cross-sectional study by (Stefanidis et al.,2015) supports laparoscopic adrenalectomy as a safer, more efficient alternative with quicker recovery and less blood loss, making it the favored option for eligible patients. However, the surgical tactic choice should also consider individual patient factors like tumor size, location, and specific surgical risks.
In a retrospective observational study (Zhu et al.,2019) analyzed 124 patients who underwent adrenalectomy for adrenal masses, dividing them according to whether they had open, robotic, or laparoscopic surgery. Most of these procedures were robotic (61.3%), followed by open (22.6%) and laparoscopic (16.1%). Incidentally discovered adrenal masses were frequent (67%), with hypertension as the most common comorbidity (53%). The study found that larger tumors, which were more ubiquitous in younger patients, correlated with a higher risk of malignancy, whereas smaller tumors tended to be functional. Robotic surgeries were noted for shorter intensive care and hospital stays.
In an prospective study by (Kebebew et al.,2015) open surgery patients often had non-functional larger adrenal masses, experienced abdominal pain, and were more likely to have surgeries on the right side. During the follow-up period, which had a median duration of 746 days (ranging from 7 to 5,840 days), there were no immediate post-operative deaths, although 8 patients eventually died across the different surgical methods. Hence (Heger et al.,2017) Laproscopic adrenalectomy was highlighted as a safe and operative alternative for benign functional adrenal tumors under 6 cm. While open surgery was preferred for larger, possibly malignant or ruptured tumors, the growing preference for robotic surgery suggests a potential departmental bias, underscoring the need for more research into long-term outcomes, risk factors, and cost implications.

LAPROSCOPIC VERSUS OPEN ADRENALECTOMY: A Critical Analysis

Laparoscopic adrenalectomy is less invasive but generally avoided for masses over 6 cm or suspected malignancy, where open adrenalectomy is preferred due to lower risk of complications like incomplete resection. In other retrospective cohort study (Zheng et al.,2018) evaluated unilateral adrenalectomy tactics in 34 patients with adrenal lesions under 10 cm. It compared ten laparoscopic, 11 transabdominal, alongside 13 posterior adrenalectomies, focusing on operative time, alongside blood loss, and hospital stay, along with postoperative analgesic needs. Operative times were similar between laparoscopic and transabdominal surgeries (212±77 min vs 174±41 min), but posterior adrenalectomy was considerably quicker (139±36 min).
In another clinical trial by (Langenhuijsen et al.,2016) Laparoscopic adrenalectomy resulted in significantly shorter hospital stays (2.1±0.9 days) compared to transabdominal (6.4±1.5 days) and posterior (5.5±2.9 days) methods and significantly less postoperative pain medication use. Despite potentially longer operative times, the laparoscopic tactic offers substantial benefits in reducing hospital stay and postoperative pain, making it the preferred option for most adrenalectomies.
In other study retrospectively (Wu et al.,2018) compared to 28 matched patients who underwent OA. LA had a 7% conversion rate to open surgery, with no deaths reported in either group. Significant differences included longer initial operative times for LA (188 vs 139 minutes, $p < 0.001$), which reduced to 130 minutes in later procedures. LA also demonstrated lower overall morbidity (16% vs 39%, $p = 0.05$), faster resumption of regular diet (2 vs 3.9 days), less meperidine usage (109 vs 209 mg), shorter hospital stays (4 vs 7.5 days), and quicker return to normal activities (2.2 vs 5.2 weeks), all statistically significant ($p < 0.001$). The study concluded that LA is a safer option than OA, offering less morbidity, shorter recovery times, and quicker returns to normalcy.
A clinical trial (Saulter et al.,2016) reviewed the medical records of 80 primary hyperaldosteronism patients who received adrenalectomy, comparing 38 open surgeries (1975-1986) to 42 laparoscopies. Open surgery patients had a longer median hypertension duration of 5 years with all showing diastolic pressures over 100 mm Hg, while laparoscopic patients had a shorter median duration of 2.5 years with 48% exceeding 100 mm Hg. Preoperative serum potassium was lower in the open surgery group (2.6 mmol/L) compared to the laparoscopic group (3.3 mmol/L), with mean serum aldosterone levels at 1.47 nmol/L and 1.30 nmol/L, respectively. Adrenal adenomas were more common in the laparoscopic group (98%) than inside the open surgery group (84%), with CT scans showing higher diagnostic accuracy for laparoscopy (93% vs. 83%). Postoperatively, 88% of laparoscopic patients normalized blood pressure versus 81% in the open surgery group, with fewer complications reported in the laparoscopic group.

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In a study (Patel, 2019) the laparoscopic group had a 9.3% conversion rate to open surgery. The mean operative time was longer for laparoscopic adrenalectomy at 150 minutes compared to 120 minutes for open surgery (p = 0.001). Infection rates were lower in the laparoscopic group at 2%, versus 6% in the open group. The average hospital stay was shorter for laparoscopic procedures, 5.1 days compared to 7.1 days for open surgery. Additionally, patients resumed oral intake quicker after laparoscopic surgery, at 1.05 days versus 2.42 days for open surgery (p = 0.001). There was no perioperative mortality inside either group. Conclusively, laparoscopic adrenalectomy, preferred for its minimal invasiveness, results in shorter hospital stays, alongside faster recovery, along with fewer complications, making it the preferred tactic for benign and selected malignant adrenal conditions.

This clinical observational study (Yousef et al.,2013) included 67 patients, with 30 undergoing OA and 37 receiving LA. Both groups had similar surgery times (OA: 203.4 minutes, LA: 192.9 minutes, p=0.776), but LA showed significantly less blood loss (104.0 mL vs. 355.0 ml, p=0.021), lower postoperative pain scores (4.5 vs. 5.6, p=0.035), and reduced analgesia demand (3.7 vs. 57.4, p<0.001). In other by (Ref) Patients in the LA group resumed oral feeding sooner (16.4 hours vs. 91.7 hours, p<0.001) and had shorter hospital stays (3.9 days vs. 8.4 days, p<0.001). Based on these results, LA is recommended as the preferred method for adrenal neoplasms, particularly for surgeons new to LA starting with cases of primary hyperaldosteronism.

In a clinical study (Sormaz et al.,2018) Figure 1 presents our algorithm for adrenal neoplasms' surgical management. If imaging suggests an adrenal mass is malignant or exceeds 6 cm, we recommend the conventional open adrenalectomy. This is because laparoscopic adrenalectomy may not be suitable for confirmed malignant lesions or those highly likely to be malignant based on imaging, due to risks like port site seeding and incomplete resection. Generally, advise against laparoscopic adrenalectomy for adrenal masses over 6 cm, as larger lesions carry a higher risk of adrenocortical carcinoma.

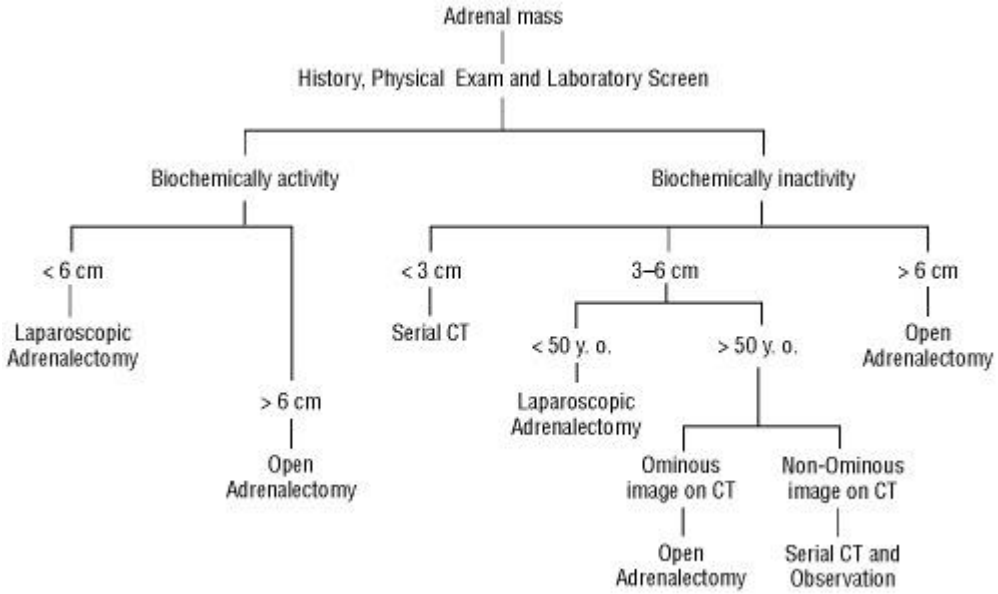

Figure 1: Surgical management (Sormaz et al.,2018)

Table I outlines the indications and benefits of choosing laparoscopic over open adrenalectomy.

Table I: Laparoscopic versus open adrenalectomy (Gaujoux et al.,2017**)**

	Size of tumor	**Abdominal survey**	**Bilateral adrenalectomy**	**For malignancy**	**Morbidity**	**Postoperative pain**		**Length of hospitalization**
Open anterior	< 15 cm	excellent one incision	feasible with	yes	moderate	+++		4 to 6 days
Open flank or posterior	≤ 5 cm	precluded	feasible with *two* incisions	yes	low	+++		3 to 5 days
Open transthoracic	> 12 cm	limited	difficult	yes		high	+++	5 to 7 days
Lap. lateral	< 8 cm	adequate	need to *reposition*	no		low	+	*1 to 3 days*
Lap. anterior	< 8 cm	adequate	need to *reposition*	no		low	+	*1 to 3 days*
Lap. posterior	< 5 cm	precluded	feasible with *bilateral trocars sites*	no		low	+	*1 to 3 days*

+++: More doses of pain medication were given (15.8 ± 6.4 doses)

+: Less doses of pain medication were given (1.4 ± 1.1 doses)

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DISCUSSION

The findings from this review highlight the significant advantages of LA over OA in the management of adrenal neoplasms. The comparable surgery times between LA and OA suggest that laparoscopic methods do not extend operative duration significantly, which is a common concern among surgeons transitioning to less invasive techniques. This systematic literature review reveals that patients with adrenocortical carcinoma (ACC) who undergo laparoscopic adrenalectomy (LA) are more likely to experience local recurrences near the primary tumor site initially.

In discussing the merits of open adrenalectomy (OA) for treating adrenocortical carcinoma (ACC), it's important to note that OA is often considered the superior tactic. The evidence suggests that OA leads to better outcomes as per overall survival, alongside disease-free survival (DFS), and lower rates of recurrence and peritoneal metastasis (Conzo et al.,2012). For instance, that tumors resected in OA were larger and had fewer positive margins compared to LA (Fassnacht et al.,2018). Moreover, after adjusting for pathologic T stage, OA patients showed significantly longer overall survival and recurrence-free survival, including specific improvements in peritoneal recurrence-free rates. These findings underscore the potential advantages of OA over LA, particularly in managing larger or more complex ACC cases. Furthermore, analysis showed no noteworthy variances in short-term survival rates between OA and LA, the long-run outcomes, notably the 5-year overall survival rate, were more favorable for the OA group. This data reinforces OA's role as the gold standard in ACC surgical treatment, with additional studies also highlighting improved short-term oncologic outcomes under this method.

The choice between open and laparoscopic techniques often hinges on tumor size and malignancy risk. The advantages of LA extend beyond smaller incisions to include less estimated intraoperative blood loss and shorter postoperative hospital stays, aligning with findings from other studies (Palazzo et al.,2016). Although operation time generally decreases with LA, it increases with tumor size, a trend also observed in another research. We found no noteworthy variances in these parameters across tumors on the left or right side, challenging the notion that right-sided surgeries are more complex. LA also tends to reduce pain and analgesia needs, with a similar or reduced overall complication rate compared to open surgery (Sautler et al.,2016). Laparoscopic adrenalectomy has been scrutinized in numerous retrospective studies, which suggest benefits such as reduced pain, better functional status, and faster recovery (Wu et al.,2018). However, these studies often lack the rigor of prospective randomized trials. Issues like biochemical outcomes and long-term effects post-adrenalectomy remain underexplored, including potential higher recurrence rates from incomplete resections.

Conclusion:

Our review demonstrates that LA offers significant advantages over OA in terms of reduced invasiveness, quicker recovery, and lower complication rates, which align with the minimally invasive tactic's benefits. However, OA remains crucial for handling larger or potentially malignant tumors due to the need for comprehensive resection and detailed exploration. The choice between LA and OA should be guided by tumor characteristics, patient condition, and surgical expertise. Further studies are recommended to refine patient selection criteria and enhance surgical techniques to expand the use of LA in managing larger adrenocortical tumors.

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