Original Article

Feasibility of laparoscopic adrenalectomy in adrenal masses greater than 5 centimeters: a systematic review and meta-analysis

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Background: Laparoscopic adrenalectomy (LA) has emerged as the primary treatment for adrenal masses. This systematic review and meta-analysis assessed LA's feasibility, safety, effectiveness, and complications for adrenal masses exceeding 5 cm.

Methods: The study was conducted using PRISMA guidelines with PROSPERO registration No. CRD42023462901. Adults with unilateral adrenal masses >5 cm who underwent unilateral LA were included. Intraoperative and postoperative measurements and complications were assessed. A systematic literature review employed a comprehensive search strategy which was last searched on September 8, 2023, through PubMed, Google Scholar, Web of Science, and ProQuest databases. Meta-analysis was utilized to analyze the outcomes. Risk of bias was assessed using the Newcastle-Ottawa scale.

Results: This systematic review encompassed 25 studies involving 963 patients who underwent LA. Tumor size varied 7.05 cm [95% confidence interval (CI): 6.24–7.70], with 50% on the right and 45% on the left. The subgroup meta-analysis comparing the transperitoneal and retroperitoneal approaches revealed the transperitoneal approach h was utilized for the largest tumor size with a mean of 12.10 cm (95% CI: 11.30–12.96), compared to the retroperitoneal approach 5.83 cm (95% CI: 5.52–6.14). Notably, the mean operative time across studies was 137.4 minutes (95% CI: 113.36–150.94), bleeding prevalence was 0.02% (95% CI: 0.01–0.03%), and average blood loss was 110.6 mL (95% CI: 78.2–156.3). Postoperative complications such as pulmonary edema, pulmonary embolism, gastric dysfunction, and wound infection were very low, ranging from 0.03% to 0.4%. Out of 963 patients, only 49 were converted to open surgery. Patient hospital stay averaged 3.72 days (95% CI: 2.97–4.66); blood transfusion was required in 1.3% (95% CI: 0.30–8.88%).

Conclusions: The feasibility and safety of LA for tumors exceeding 5 cm in size have notable implications for intraoperative and postoperative outcomes. Underreporting in the included studies may impact the generalizability of findings.

Keywords: Laparoscopic adrenalectomy (LA); feasibility; large adrenal masses; transperitoneal and retroperitoneal approaches

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Introduction

Throughout the last decade, laparoscopic adrenalectomy (LA) has become the main treatment option for adrenal masses since minimally invasive surgery was introduced (1). It can be done through different approaches; however, laparoscopic transabdominal lateral adrenalectomy is the predominant form of surgery which is more familiar to most surgeons globally (2).

Adrenalectomy is indicated when there is a suspicion of malignancy or malignant tumors are present, as well as for non-functional tumors with malignancy risk (3). Numerous studies have shown the feasibility and safety of laparoscopic techniques for the removal of pheochromocytomas, since in 1992 first reported a lateral transabdominal LA approach (4).

While LA is the gold standard for managing small adrenal masses, its application for larger lesions (>5 cm) remains controversial due to concerns about technical feasibility, oncological safety, and limited high-quality evidence (5) Therefore, a systematic review and meta-analysis was carried out to comprehensively assess the existing literature, address knowledge gaps, and inform clinical practice, which ultimately impact patient care by establishing the efficacy and safety of LA for large masses. This study was conducted to evaluate the feasibility of LA in adrenal masses greater than 5 cm in terms of safety, effectiveness, and complications. We present this article in accordance with the PRISMA reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-69/rc) (6).

Highlight box

Key findings

- The proportion of tumors on the right side was 50% while on the left side, it was 45%. The transperitoneal approach exhibited a larger mean tumor size compared to the retroperitoneal approach.
- Retroperitoneal approach demonstrated a shorter mean operative time of 97.56 minutes.
- The conversion rate to open surgery is more in transperitoneal approach.
- The transperitoneal approach had a bleeding rate of 3.24% whereas the retroperitoneal approach had a slightly higher bleeding rate of 5.88%.

What is known and what is new?

- Laparoscopic adrenalectomy (LA) has become the main treatment option for adrenal masses.
- This systematic review and meta-analysis assessed LA's feasibility, safety, effectiveness, and complications for adrenal masses exceeding 5 cm.

What is the implication, and what should change now?

- Therefore, this systematic review approves that larger tumor generally correlated with longer operative times, and the transperitoneal approach was associated with increased operative duration. Conversion to open surgery significantly impacted safety, emphasizing the need for careful consideration.

Methods

Study eligibility criteria

Local institutional ethical approval was not required as all data used in this analysis were obtained from a previously published resource. This study was prospectively registered with the International Prospective Register of Systematic Reviews and Meta-Analysis by one of the authors (Lama Alzelfawi) (PROSPERO: CRD42023462901).

For inclusion in this analysis, studies had to meet the following inclusion criteria: case-control studies, retrospective cohort studies, and prospective cohort studies published in English language. Adults with unilateral adrenal masses larger than 5 cm who went through laparoscopic unilateral adrenalectomy, including these approaches, transperitoneal, transabdominal, retroperitoneoscopic, and retroperitoneal adrenalectomy, were included. Studies failing to meet these strict eligibility criteria were excluded. The reasons for study exclusion were as follows: irrelevant intervention, i.e., bilateral adrenalectomy robotic, transvaginal, or open laparotomy, irrelevant subjects, i.e., adult patients with adrenal mass less than 5 cm, pediatric population, and animal studies, inadequate data reporting, wrong study design, repetitive publications, language limitation; and non-availability of the full text.

The main outcomes of this systematic review were safety and effectiveness. Additionally, intraoperative and postoperative measurements were tumor size, lesion localization (right/left), estimated blood loss, operation time, and hospital stay.

Complications were divided into intra-operative complications and post-operative complications. Intra-operatively, hemodynamic instability, adrenal vein avulsion, conversion to open surgery, hypotension/hypertension, estimated blood loss. Postoperatively, wound infection,

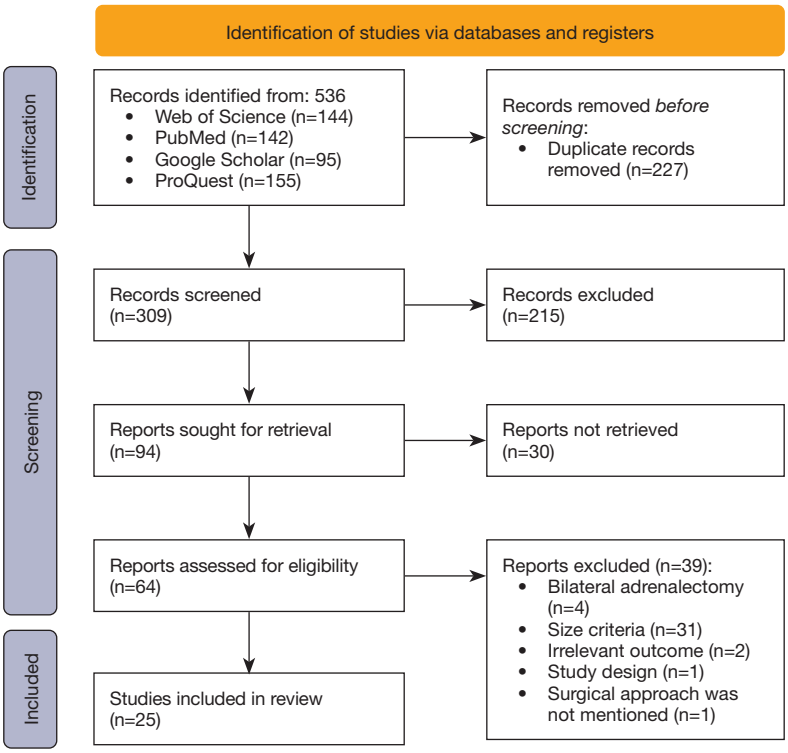

Figure 1 PRISMA flow diagram.

gastroenteric dysfunction, bleeding, and mass recurrence.

Information sources and search strategy

A systematic review and meta-analysis of the literature were performed by a broad electronic search through PubMed, Google Scholar, Web of Science, and ProQuest databases for all relevant articles published in English for more than 5 cm adrenal tumors as shown in *Figure 1*. This study does not have restrictions toward date. Each database was initially searched for relevant titles. This search was performed by two independent reviewers, using a predetermined search strategy that was designed by the senior authors. The keywords used were safety, effectiveness, complications, feasibility, large adrenal mass, and LA.

Selection process, data collection process and analysis

All articles from the primary search were imported to Rayyan (7) for duplication removal and independently screened by two authors (E.A. & Lama Alzelfawi) based on title and abstract. Four authors reviewed the full text of all studies (E.A., Lena AlDosari, Z.A., & A.A.). Retrieved studies were reviewed to ensure inclusion criteria were met for the primary outcome at a minimum, with discordances in opinion resolved through consultation with the third reviewer (B.A.). By reading the title and abstract and applying the inclusion/exclusion criteria. Disagreements at any step of the screening process were handled through debate and consensus among all authors. The data was manually independently extracted by five authors (Lama Alzelfawi, E.A., Lena AlDosari, Z.A., & A.A.). An Excel sheet was used that included patients' data and demographics (age, gender), study characteristics (main author's name, year of publication, country, study design, sample size), intraoperative measurements (tumor size, tumor localization, estimated blood loss, operation time), intra-operative complications (hemodynamic instability, conversion to open, adrenal vein avulsion), and postoperative complications (bleeding, pulmonary embolism, pulmonary edema, blood transfusion, gastroenteric dysfunction, wound infection, mass recurrence). Tables were used to demonstrate included studies characteristics and results. The PRISMA chart flow figure was used to show the process of study selection. Moreover, forest plots were utilized to illustrate each outcome.

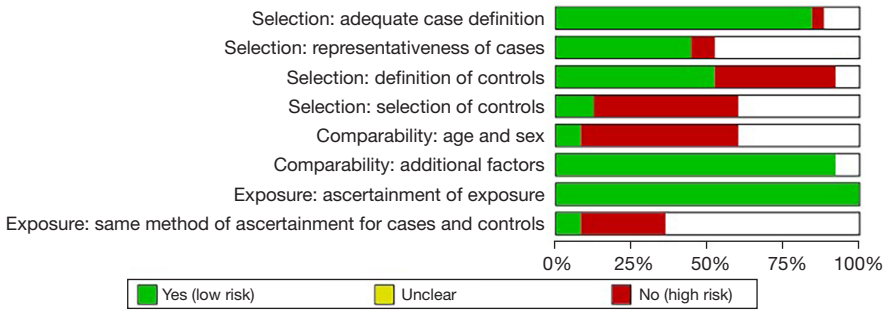

Figure 2 Risk of bias graph.

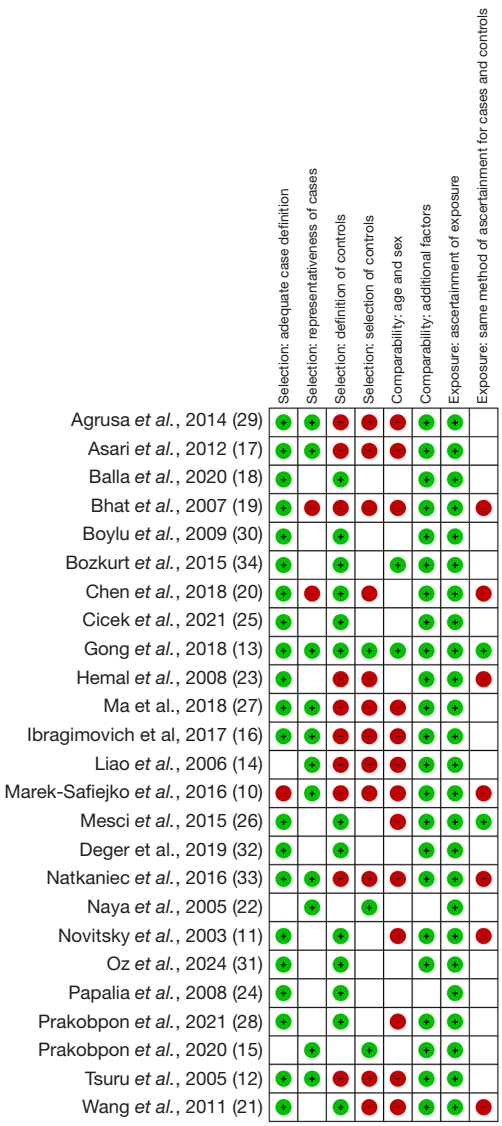

Figure 3 Risk of bias summary, review authors' judgments about each risk of bias item for each included study (10-34). +, low risk; –, high risk.

Meta-analysis was performed by random-effect models using R Studio with Meta Package (8).

Data items

The combinations and terms used included ("Adrenal Tumors Greater than" OR "Adrenal Tumors larger than" OR "Adrenal Masses Greater than" OR "Adrenal Masses larger than" OR "Adrenal Tumors >5 cm" OR "Adrenal Tumors" OR "Adrenal Masses") AND ("transperitoneal adrenalectomy" OR "laparoscopic transabdominal adrenalectomy" OR "laparoscopic transperitoneal adrenalectomy" OR "retroperitoneoscopic adrenalectomy" OR "retroperitoneal adrenalectomy". The search terms were identified in the title, abstract or medical subject heading.

Risk of bias

The observational studies' methodological quality was assessed using the Newcastle-Ottawa scale (9), by three independent reviewers (Lama Alzelfawi, Lena AlDosari, Z.A.) with conflict resolution achieved through mutual consensus or, if necessary, involvement of a third party. The assessment comprised three sections, totaling nine components, examining study population selection, comparability of factors, and exposure ascertainment. Each section featured 2 to 4 questions, rated as high, low, or unclear risk of bias. Discrepancies in ratings underwent resolution through discussion among reviewers, with external mediation available if disagreements persisted. *Figures 2,3* provide a comprehensive risk of bias graph and summary, revealing generally low bias risk in study selection domains, such as adequate case definition. However, comparability and exposure ascertainment displayed extremely low or negligible bias risk. Conversely,

Table 1 Characteristics of included studies and patient demographics

Serial number	Author	Year	Country/region	Study design	Sample size	Intervention
1	Marek-Safiejko *et al.* (10)	2016	Poland	Retrospective review	27	Lateral transperitoneal LA
2	Novitsky *et al.* (11)	2003	United States	Retrospective review	24	Lateral transperitoneal LA
3	Tsuru *et al.* (12)	2005	Japan	Retrospective analysis	29	Lateral transperitoneal LA
4	Gong *et al.* (13)	2018	China	Retrospective cohort	18	Retroperitoneal LA
5	Liao *et al.* (14)	2006	Taiwan	Retrospective cohort	39	Lateral transperitoneal LA
6	Prakobpon *et al.* (15)	2020	Thailand	Retrospective cohort	48	Transperitoneal LA
7	Ibragimovich *et al.* (16)	2017	Uzbekistan	Comparative case study	15	Lateral transabdominal LA
8	Asari *et al.* (17)	2012	Australia	Retrospective study	37	Transperitoneal endoscopic adrenalectomy
9	Balla *et al.* (18)	2020	Italy	Case-control study	81	Anterior transperitoneal LA
10	Bhat *et al.* (19)	2007	India	Prospective study	9	Anterolateral transperitoneal LA
11	Chen *et al.* (20)	2018	China	Retrospective study	78	Retroperitoneal LA
12	Wang *et al.* (21)	2011	China	Retrospective study	110	Retroperitoneoscopic adrenalectomy
13	Naya *et al.* (22)	2005	Japan	Retrospective study	16	Transperitoneal and retroperitoneal lateral LA
14	Hemal *et al.* (23)	2008	India	Retrospective study	22	Transperitoneal and retroperitoneal LA
15	Papalia *et al.* (24)	2008	Italy	Retrospective study	40	Right transperitoneal LA
16	Cicek *et al.* (25)	2021	Turkey	Retrospective study	53	Transperitoneal LA
17	Mesci *et al.* (26)	2015	Turkey	Retrospective study	76	Transperitoneal LA
18	Ma *et al.* (27)	2018	China	Comparative study	17	Retroperitoneoscopic and transperitoneal LA
19	Prakobpon *et al.* (28)	2021	Thailand	Retrospective study	48	Transperitoneal LA
20	Agrusa *et al.* (29)	2014	Italy	Prospective study	14	Transperitoneal LA
21	Boylu *et al.* (30)	2009	United States	Retrospective study	8	Transperitoneal LA
22	Öz *et al.* (31)	2024	Turkey	Retrospective cohort study	33	Transperitoneal LA
23	Değer *et al.* (32)	2019	Turkey	Retrospective study	16	Observational study
24	Natkaniec *et al.* (33)	2016	Poland	Retrospective study	89	Lateral transperitoneal LA
25	Bozkurt *et al.* (34)	2015	Turkey	Retrospective study	16	Transabdominal LA

LA, laparoscopic adrenalectomy.

other aspects demonstrated a higher average risk of bias, underscoring the critical assessment needed in observational research.

Results

Across the 25 studies, a comprehensive analysis of 963 patients who underwent LA for large adrenal masses revealed diverse demographic characteristics, the types of intervention, the included studies utilized various approaches for LA, as shown in *Table 1*. The transperitoneal LA (TLA) approach was the more prevalent choice, applied in most cases across various studies.

Intraoperative measurements

Tumor sizes varied widely in the study, as demonstrated in *Table 2*. Additionally, the proportion of tumors on the right side was 50% (0.50) [95% confidence interval (CI): 0.471–0.543], while on the left side, it was 45% (0.45) (95% CI: 0.404–0.508). The subgroup meta-analysis comparing the transperitoneal and retroperitoneal approaches for

Table 2 Intraoperative and post-operative measurements

Serial number	Author	Tumor size (cm)	Right side tumor (N)	Left side tumor (N)	Estimated blood loss (mL)	Operation time (minutes)	Hospital stay (days)
1	Marek-Safiejko *et al.* (10)	6.1±2.1	12	15	142.1±127.6	153.1±50.4	2.67±1.01
2	Novitsky *et al.* (11)	6.8±1.5	12	12	87±69	178±55	2.5±1.9
3	Tsuru *et al.* (12)	6.5	16	13	136.6	176±48	0
4	Gong *et al.* (13)	9.9±2.1	11	7	247.2±274.1	176.3±49.7	6.3±1.4
5	Liao *et al.* (14)	6.2±1.2	23	16	75±79	207	4.2±1.8
6	Prakobpon *et al.* (15)	NA	26	22	100	120	9
7	Ibragimovich *et al.* (16)	7.1±0.8	10	5	117±38	115.3±9.6	5.8±1.2
8	Asari *et al.* (17)	8.72±2.4.1	16	21	0	181.3±74.5	0
9	Balla *et al.* (18)	6.9±1.4	35	46	0	101.4	4.6±2.4
10	Bhat *et al.* (19)	8±1.47	4	5	105.9	142.7	4.1
11	Chen *et al.* (20)	5.81±1.17	29	11	33.72±21.34	98.71±32.30	7.43±2.82
12	Wang *et al.* (21)	7.2±2.1	62	48	81.3±46.1	70.8±18.6	5.6±1.4
13	Naya *et al.* (22)	NA	5	11	212±165	210±69	0
14	Hemal *et al.* (23)	7.85±2.1	10	12	LTP 132.33; LRP 94.28	LTP 149.33; LRP 132.1	LTP 3.5; LRP 3.28
15	Papalia *et al.* (24)	AT 6.52; LT 6.59	40	40	AT 100; LT 105.3	AT 75.25; LT 84.75	AT 3.5; LT 3
16	Cicek *et al.* (25)	AT 8.75±4.08; LT 6.73±1.84	28	25	86±70.4	101.6±39.9	3.7±3.5
17	Mesci *et al.* (26)	5.37±2.44	42	34	114	112.2±46.7	2.5±0.7
18	Ma *et al.* (27)	5.63±2.39	12	5	50	83.6±23.1	5.4±1.7
19	Prakobpon *et al.* (28)	8	26	22	100	120	5.5
20	Agrusa *et al.* (29)	8.2	8	6	90	181	4.2
21	Boylu *et al.* (30)	12.1±1.2	6	2	334.38±85.3	188.75	2.12±1.6
22	Öz *et al.* (31)	6.7	12	21	55.30±34.35	90	3.4±0.9
23	Değer *et al.* (32)	6.4±3.5	10	6	94.3	107.4±25.4	2.075±0.95
24	Natkaniec *et al.* (33)	7.76±2.1	43	44	172.8	111.9±43.7	0
25	Bozkurt *et al.* (34)	9.17±18.6	8	8	100.5±40.1	113.4±41.0	2±0.8

Data are presented as mean ± SD or n as appropriate. NA, not applicable; LTP, laparoscopic transperitoneal; LRP, laparoscopic retroperitoneal; AT, anterior transperitoneal; LT, lateral transperitoneal; SD, standard deviation.

adrenalectomy revealed the transperitoneal approach was utilized for the largest tumor size with a mean of 12.10 cm (95% CI: 11.30–12.96).

This significant difference was supported by a test for subgroup differences (P<0.01), indicating that the tumor size differs significantly based on the surgical approach *Figure 4*. The operating time data across the reviewed studies exhibit variability in the duration of the surgical procedures. Marek-Safiejko *et al.*, reported a mean total operative time of 153.1 minutes (10), while Novitsky *et al.*, had presented an average operating time of 178±55 minutes (11). The results of random effect model for subgroup meta-analysis showed the retroperitoneal approach demonstrated a mean operative time of 140.2 minutes (95% CI: 84.45–232.98),

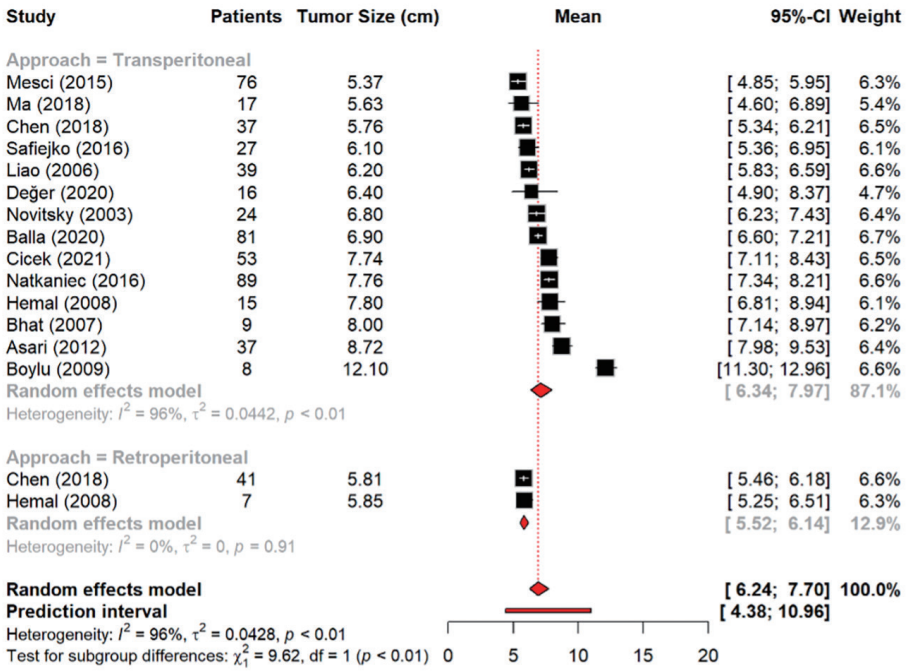

Figure 4 Subgroup analysis of tumor size based on transperitoneal laparoscopic adrenalectomy and retroperitoneal laparoscopic adrenalectomy approaches. CI, confidence interval.

while the transperitoneal approach required a mean operative time of 138.9 minutes (95% CI: 118.29–163.24). There was insignificant difference supported by a test for subgroup differences (P=0.97), suggesting that no advantages in terms of operative time between two approaches *Figure 5*. Moreover, Chen *et al.*, study highlighted the difference in operating time between the retroperitoneal LA (RLA) approach (98.70±32.30 minutes) while the TLA approach has a longer operating time (124.36±34.62 minutes) (20). In addition, Ma *et al.* has observed variations in mean operative times, with TLA having the longest duration at 83.6±23.1 minutes and RLA the shortest at 49.7±13.4 minutes (27). The data collectively reflects the diverse range of operating times associated with different approaches and procedures, emphasizing the need for careful consideration of these variations in the context of the surgical interventions under investigation. Estimated blood loss during LA for adrenal masses exceeding 5 cm varied across the reviewed studies in *Figure 6*. The variations in blood loss are crucial indicators of the procedural intricacies and potential challenges associated with the laparoscopic approach for larger adrenal masses. Postoperative measurements in our study included hospital length stay which varied across studies in the systematic literature review, as shown in *Table 2*.

Conversely, the average blood loss was 110.6 mL (95% CI: 78.2–156.3), with a wide range of 33.7 to 334.3 mL and substantial heterogeneity (I^2=98%).

As shown in *Figure 6B*, the analysis of blood loss revealed that the transperitoneal approach resulted in a substantially higher mean blood loss of 106.9 mL (95% CI: 67.42–169.75), compared to the retroperitoneal approach which showed a lower mean blood loss of 80.98 mL (95% CI: 14.14–463.67). This significant difference was supported by a test for subgroup differences (P<0.01), suggesting that the retroperitoneal approach may lead to less blood loss during surgery.

Notably, patients exhibited an average hospital stay of 3.72 days (95% CI: 2.97–4.66), ranging from 2 to 7.4 days, illustrated in *Figure 7A*. There was no significant difference in mean hospital stay between the two approaches. While the retroperitoneal approach tended to have a slightly longer mean hospital stay of 4.91 days (95% CI: 2.15–11.22) compared to 4.59 days (95% CI: 2.46–8.58) for the transperitoneal approach, this difference was not statistically significant (P=0.90). Regarding the comparison of conversion rates to open surgery between the transperitoneal and retroperitoneal approaches yielded interesting findings in *Figure 7B*.

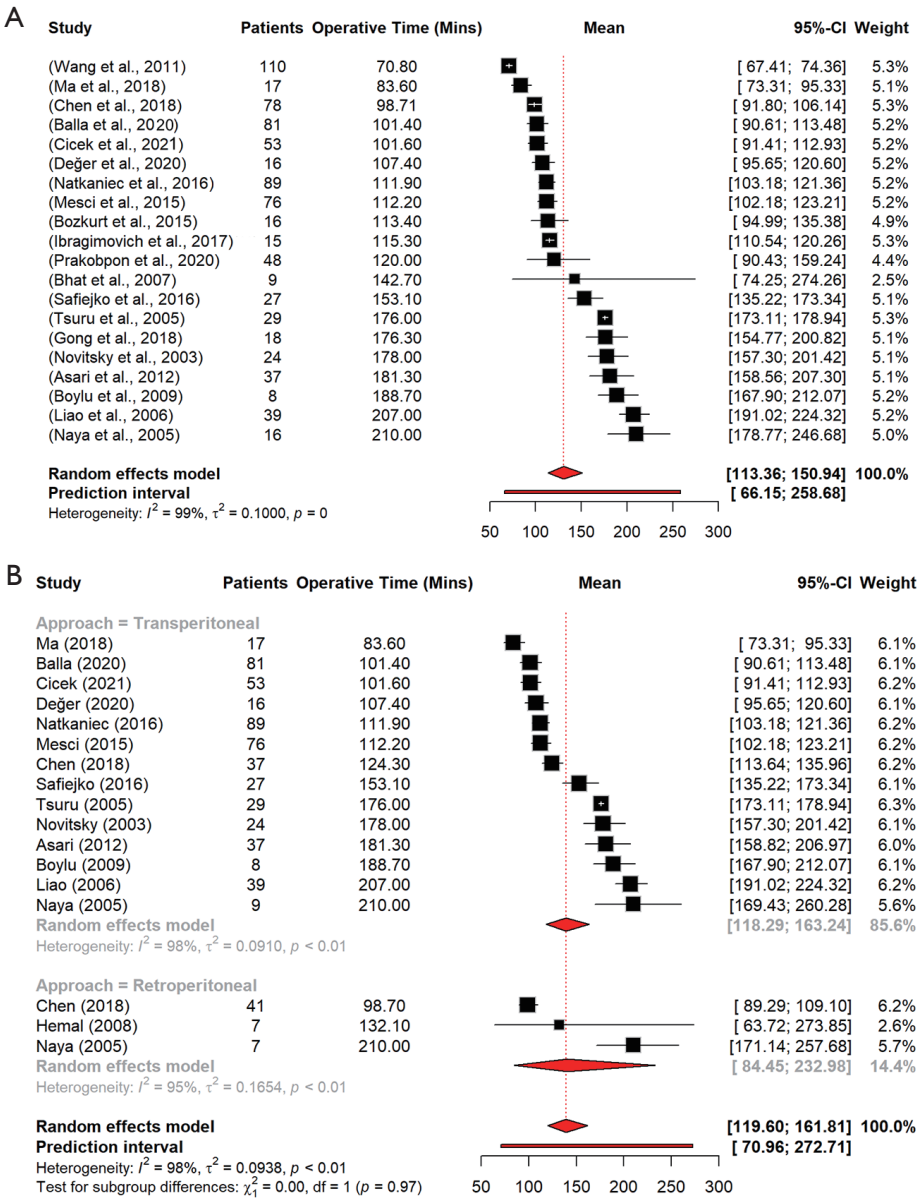

Figure 5 Operative time in minutes. (A) Overall operating times across all studies; (B) subgroup analysis of operative time based on transperitoneal laparoscopic adrenalectomy and retroperitoneal laparoscopic adrenalectomy approaches. CI, confidence interval.

Regarding intra-operative complications, adrenal vein avulsion, hemodynamic instability, and conversion to open surgery were included.

Only one study reported 1 case of adrenal vein avulsion (30). In addition, hemodynamic instability was defined in our study as blood pressure fluctuations during the operation, which was reported in two studies. Only seven patients out of 963 cases experienced hemodynamic instability, as shown in *Figure 8*. The conversion to open surgery in LA surgeries varies across studies. Out of 963 patients, 49 were converted to open surgery. Regarding the comparison of conversion rates to open surgery between the transperitoneal and retroperitoneal approaches yielded interesting findings *Figure 9A*. For the transperitoneal approach, the proportion of cases converted to open surgery was 7% (95% CI: 4–10%), while for the retroperitoneal approach, this proportion was notably lower at 2% (95% CI: 0–4%). The test for subgroup differences indicated a significant

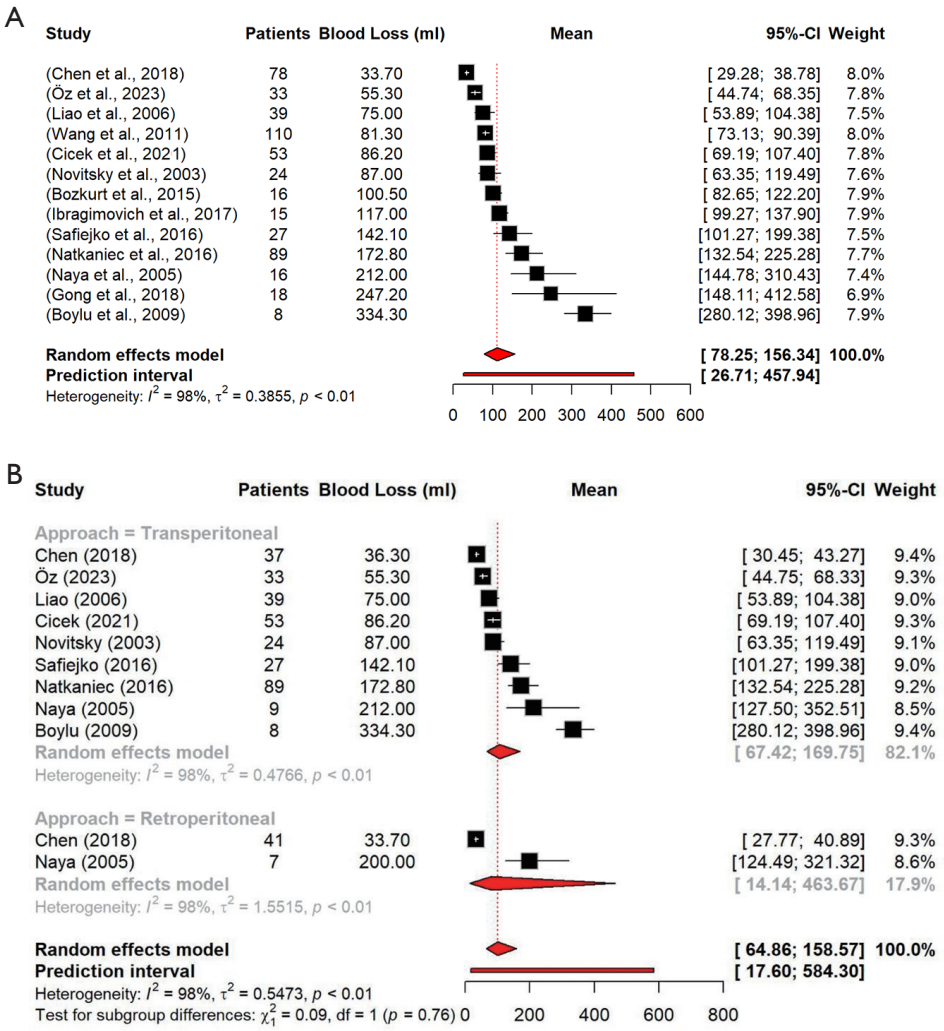

Figure 6 Estimated blood loss. (A) The forest plot shows the overall estimated blood loss across all the included studies; (B) sub-analysis based on transperitoneal laparoscopic adrenalectomy and retroperitoneal laparoscopic adrenalectomy approaches. CI, confidence interval.

variation between the groups (P=0.01), suggesting that the conversion rate to open surgery is more in transperitoneal approach *Figure 9B*.

Specific factors like severe adhesions, and tumor characteristics contributed to conversions. Successful laparoscopic outcomes without conversion were seen in 13 studies. Hemodynamic instability and open conversion rates were infrequent, reported at 0.00 (95% CI: 0.00–0.01, I^2=0%) and 0.03 (95% CI: 0.01–0.04, I^2=48%) respectively as shown in *Figures 8*,*9*.

Post-operative complications

Postoperative complications included pulmonary embolism, pulmonary edema, gastrointestinal dysfunction, bleeding, blood transfusion, mass recurrence, and wound infection. In terms of postoperative complications, the analysis revealed low prevalence rates for adverse events following LA. Pulmonary edema, gastric dysfunctions, wound infection, pulmonary embolism, and mass recurrence were reported at 0.03%, 0.04%, 0.4%, 0.03%, and 0.03% respectively. These findings collectively highlight the favorable postoperative outcomes associated with laparoscopic procedures for adrenal resection. Furthermore, one study reported mass recurrence in two patients (17). Blood transfusion was required in 1.3% of cases, while bleeding was reported in 35 cases (*Table 3*).

Figure 10 shows a total of 12 patients who had

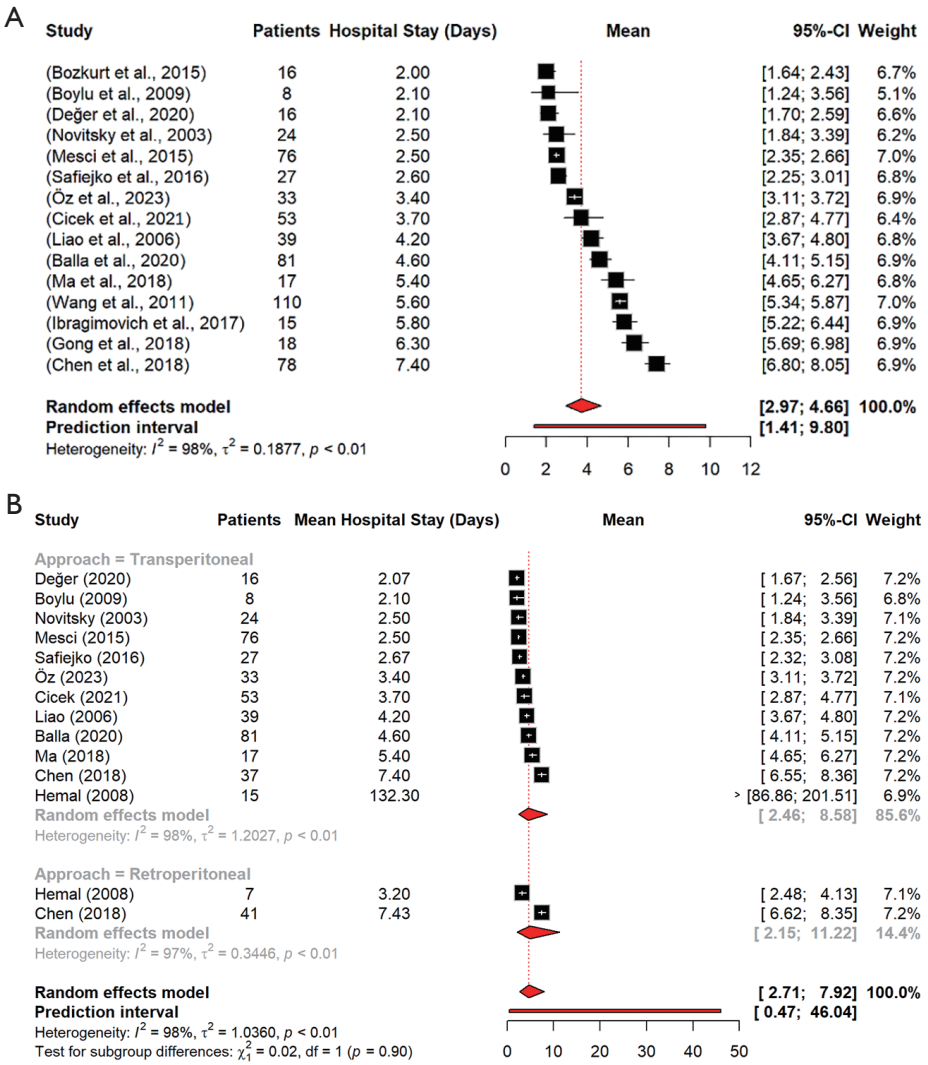

Figure 7 Hospital length of stay in days. (A) Overall hospital length of stay across all studies; (B) subgroup analysis of hospital stay based on transperitoneal laparoscopic adrenalectomy and retroperitoneal laparoscopic adrenalectomy approaches. CI, confidence interval.

postoperative wound infections.

Figure 11 shows blood transfusion was required in) 1.0% (0.01) of cases (95% CI: 0.00–0.02), with a wide range from 0% to 31%, accompanied by high heterogeneity (I^2=51%).

The prevalence of bleeding during laparoscopic surgery was notably low at 2% (0.02) (95% CI: 0.01–0.03), with a range from 0% to 12% as shown in *Figure 12*.

As shown in *Figure 12B*, regarding the proportion of bleeding, the transperitoneal approach had a bleeding rate of 3% (0.03) (95% CI: 0.01–0.05), whereas the retroperitoneal approach had a slightly higher bleeding rate of 6% (0.06) (95% CI: 0.02–0.10). However, the test for subgroup differences did not show a significant variation between the two approaches (P=0.28).

Discussion

The adrenalectomy approach has evolved from an open procedure requiring large incisions to a minimally invasive approach that entails a much smaller incision (3). The diverse demographic characteristics of the 963 patients across 25 studies undergoing LA for adrenal masses more significant than 5 cm underscore the need to tailor surgical approaches to individual patient profiles. A comprehensive preoperative study is necessary for evaluating all adrenal masses, which involves clinical evaluation, hormonal

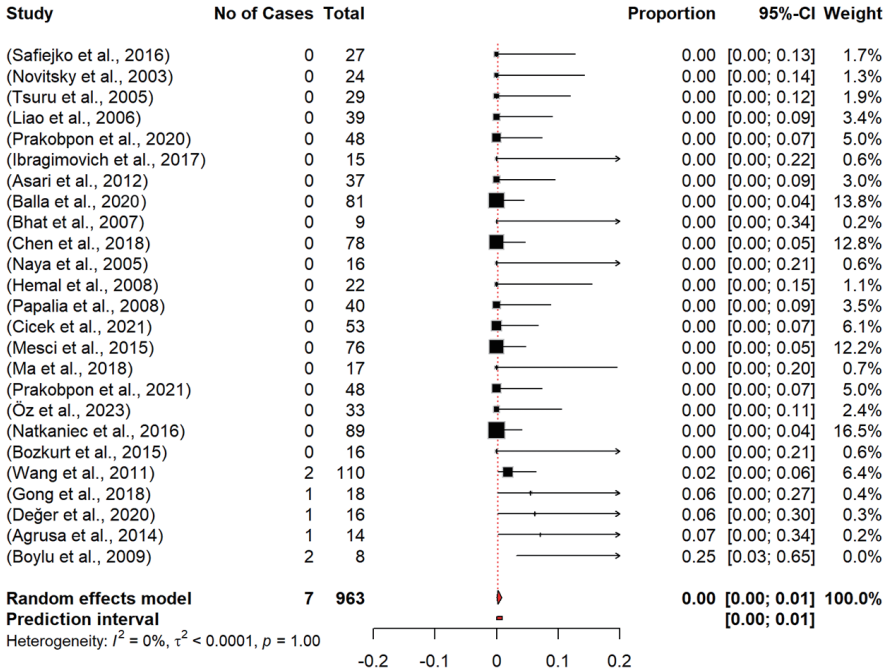

Figure 8 Occurrence of hypotension/hypertension. CI, confidence interval.

assessment and imaging. Specific imaging techniques like scintigraphy or positron emission tomography may be used for suspected pheochromocytoma cases. The most important factors to evaluate during preparation were the underlying cause and the patient's condition. After care and post-operative evaluation also highly relied on the underlying pathology. All patients were transferred to a recovery room for the first 4–6 h after surgery, to monitor their condition. Moreover, each patients' post-surgery care plan depended on the procedural outcome and intra/post operative complications (35).

Since adrenal tumors are relatively rare, technical skills in laparoscopic surgery play a crucial part. Many surgeons have limited experience in handling them. The choice of surgical approach depends on factors such as tumor size, patient's body type, and the surgeon's expertise (36).

Intraoperative and postoperative complications represent crucial aspects of LA for adrenal masses exceeding 5 cm, and a deeper exploration of these outcomes is paramount for a comprehensive understanding (37,38). While our systematic review highlighted the underreporting of tumor rupture instances, the available data underscores the need for documentation to ascertain this complication's actual occurrence or absence. Moreover, the inconsistent reporting of hypotension and hypertension during the procedure suggests a significant gap in understanding the hemodynamic stability associated with LA (39). Future studies should prioritize standardized reporting to facilitate a more detailed analysis of intraoperative complications, enabling the identification of potential risk factors and optimization of patient care strategies.

The considerable variability in operating times across studies underscores the complexity of LA for larger adrenal masses. Factors such as the surgical approach, tumor size, and the pathological diagnosis (pheochromocytoma) contribute to this diversity (40).

Several factors emerged across the studies as influential in determining operative time. Tumor size significantly impacts operative time, with larger masses associated with prolonged procedures (28). Tumor size, particularly when ≥8 cm, was a significant factor impacting operative time, as concluded by Öz *et al.*, a longer operative time for masses ≥8 cm compared to smaller masses (31). Diagnosing pheochromocytoma further contributes to extended operative times (41).

A variety of factors contributed to the decision to convert to open surgery, including severe adhesions and tumor characteristics (34). The conversion to open surgery occurred in 49 patients out of the total of 963 patients, and all the factors contributing to conversion were not

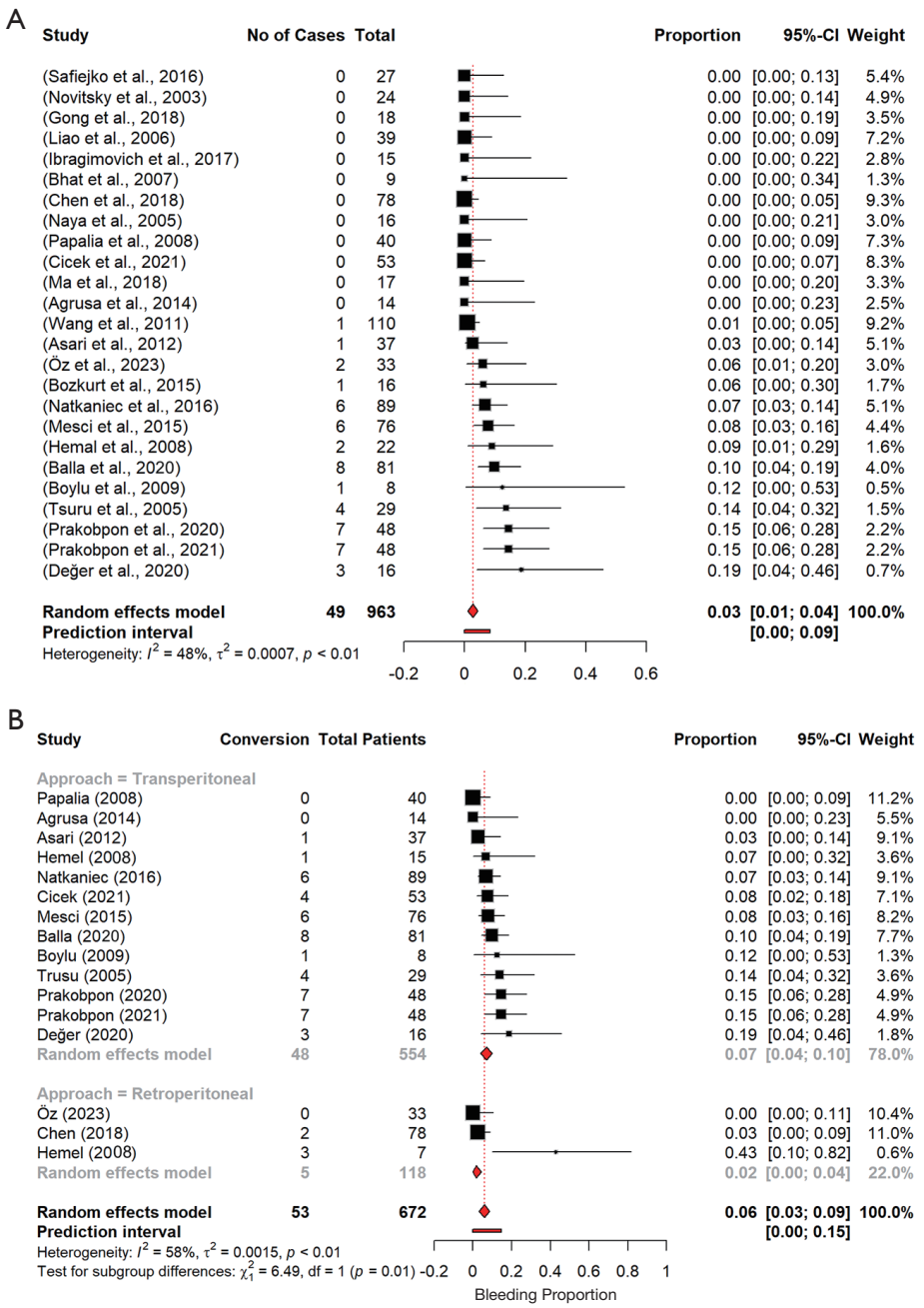

Figure 9 Conversion to open surgery. (A) Overall conversion to open surgery across studies; (B) subgroup analysis of conversion rate based on transperitoneal laparoscopic adrenalectomy and retroperitoneal laparoscopic adrenalectomy approaches. CI, confidence interval.

attributed to the tumor size. Successful outcomes without conversion in some studies underscore the critical role of preoperative assessment and surgical expertise (42,43). Variability in estimated blood loss across studies highlights the importance of considering factors like tumor size and surgical approach (44). Ibragimovich *et al.* reported a mean of 117±38 mL, while Naya *et al.* noted a mean of 212±165 mL (16,22).

Turning our attention to postoperative outcomes, which are integral to evaluating the overall success and safety of

Table 3 Post-operative complications

Serial number	Author	Year	Bleeding (mL)	Blood transfusion (units)
1	Marek-Safiejko *et al.* (10)	2016	0	4
2	Tsuru *et al.* (12)	2005	0	1
3	Gong *et al.* (13)	2018	1	1
4	Prakobpon *et al.* (15)	2020	5	10
5	Asari *et al.* (17)	2012	1	1
6	Balla *et al.* (18)	2020	3	4
7	Bhat *et al.* (19)	2007	0	1
8	Chen *et al.* (20)	2018	5	0
9	Papalia *et al.* (24)	2008	1	0
10	Cicek *et al.* (25)	2021	0	1
11	Mesci *et al.* (26)	2015	5	0
12	Prakobpon *et al.* (28)	2021	4	10
13	Agrusa *et al.* (29)	2014	1	0
14	Boylu *et al.* (30)	2009	1	1
15	Öz *et al.* (31)	2024	2	0
16	Değer *et al.* (32)	2019	0	1
17	Natkaniec *et al.* (33)	2016	6	4
18	Bozkurt *et al.* (34)	2015	0	5

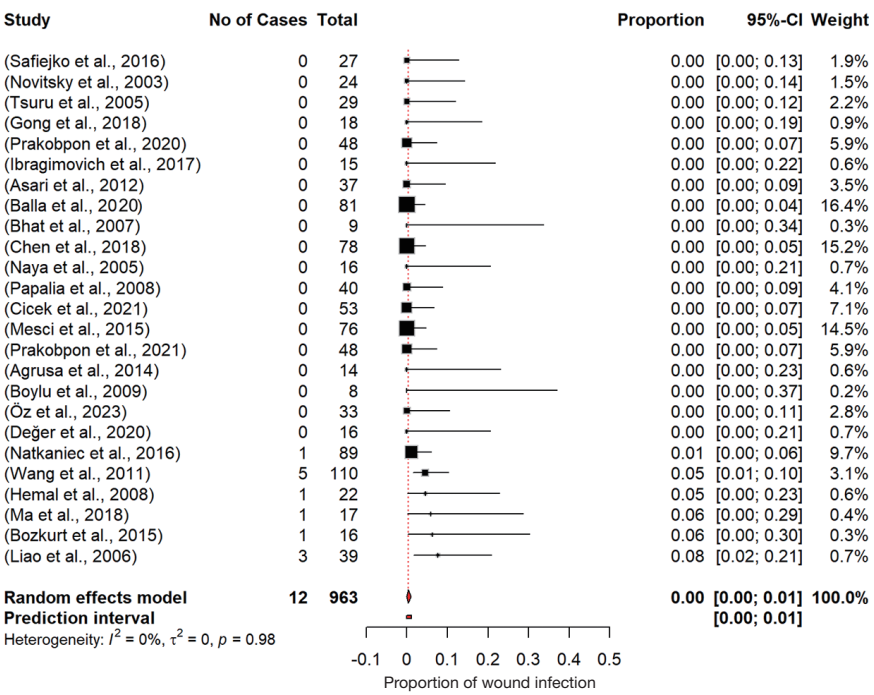

Figure 10 Occurrence of wound infection. CI, confidence interval.

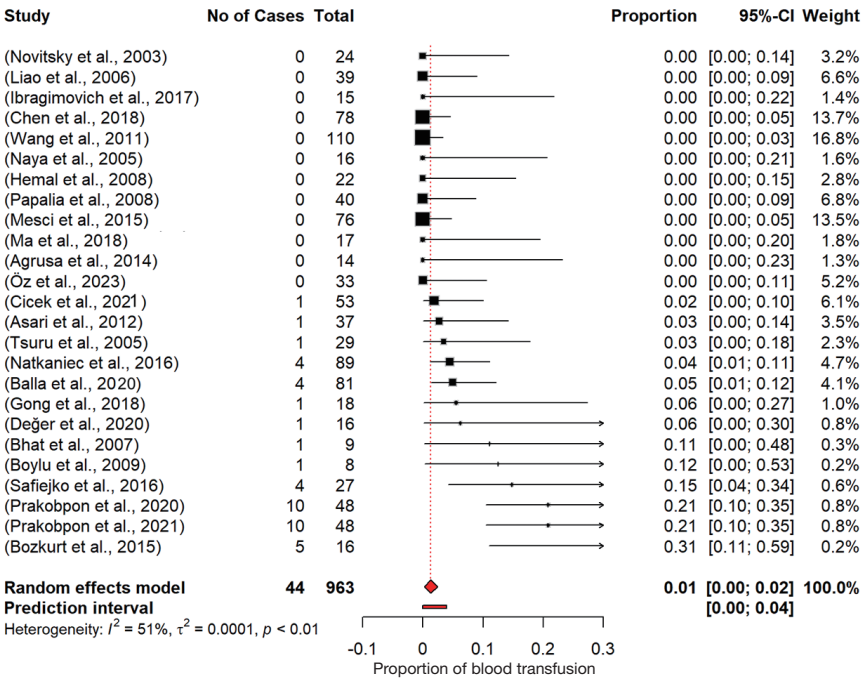

Figure 11 Blood transfusion. CI, confidence interval.

LA, a low prevalence of postoperative complication was observed by the overall reported complications; gastroenteric dysfunction was encountered in one case (28), pulmonary embolism was as well encountered in one case (12), pulmonary edema was seen in two cases (10,19). In contrast, wound infection has been reported in 12 cases (14,21,23,27).

The heterogeneity in hospital length of stay (LOS) across different studies, with LOS ranging from 2 to 7 days, factors such as the surgical approach (e.g., retroperitoneal *vs.* transabdominal), and tumor size may contribute to variations in recovery times (45,46). Novitsky *et al.* reported an average length of stay of 2.5±1.9 days (11). Tsuru *et al.* indicated a more prolonged recovery for large-tumor patients (5.4 *vs.* 4.5 days) (12).

Critical gaps in the literature, such as underreported intraoperative complications and varying conversion rates to open surgery, highlight the urgent need for standardized and comprehensive documentation to accurately evaluate the safety and feasibility of the procedure.

The overarching theme of our systematic review and meta-analysis revolves around the safety and feasibility of LA for larger adrenal masses. While the procedure demonstrated feasibility, findings revealed varying safety outcomes. Factors influencing safety included tumor size, surgical approach, and the occurrence of complications. Larger tumors generally correlated with longer operative times, and the transperitoneal approach was associated with increased operative duration. Conversion to open surgery significantly impacted safety, emphasizing the need for careful consideration.

Certain limitations should be acknowledged. The inherent heterogeneity across the included studies, ranging from variations in patient populations to diverse surgical techniques, introduces a level of variability that may impact the generalizability of the findings. The limited availability of detailed data in some studies, particularly regarding intraoperative complications and postoperative outcomes, hindered a comprehensive analysis.

Conclusions

In conclusion, the feasibility and safety of LA for tumors larger than 5 cm have a significant impact on several intraoperative and postoperative outcomes. Larger masses and transperitoneal approaches require a longer operation time. Conversion to open surgery was related to tumor characteristics and the presence of adhesions. Regarding hemodynamic instability, it was low among patients. These complications differ among several studies, indicating many factors affecting laparoscopic safety.

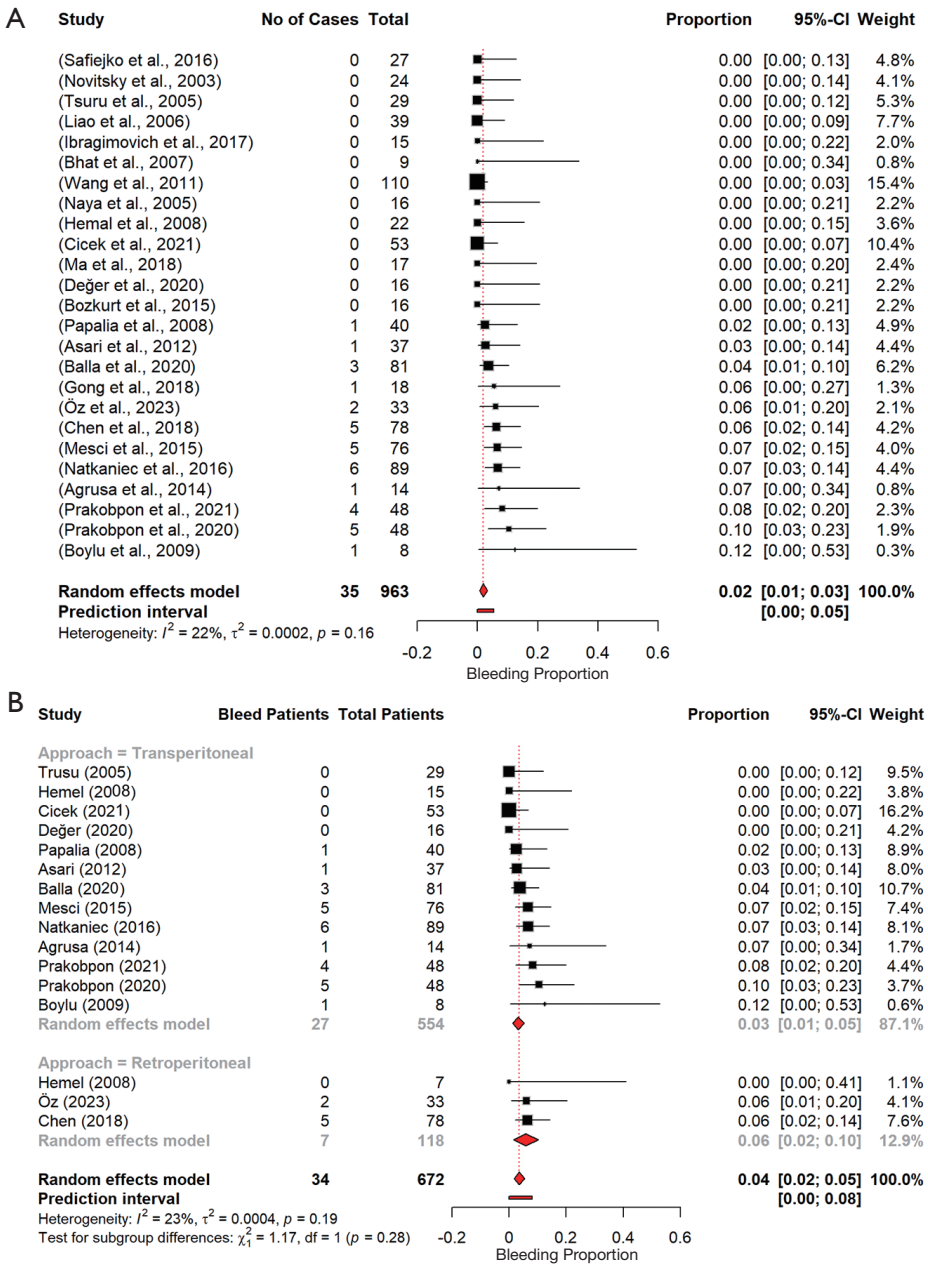

Figure 12 Intra-operative bleeding. (A) Overall intra-operative bleeding across studies; (B) subgroup analysis of bleeding proportion based on transperitoneal laparoscopic adrenalectomy and retroperitoneal laparoscopic adrenalectomy approaches. CI, confidence interval.

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Footnote

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