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RESEARCH

Posterior retroperitoneal versus transperitoneal laparoscopic adrenalectomy in adults: results from the EUROCRINE® surgical registry

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Abstract

Purpose This study aims to compareposterior retroperitoneal laparoscopic adrenalectomy (PRLA) and laparoscopic transperitoneal adrenalectomy (LTA) in adults using pan-European data as conflicting results have been published regarding length of hospital stay, institutional volume, and morbidity.

Methods This retrospective cohort study analyzed data from the surgical registry EUROCRINE®. All patients undergoing PRLA and TLA for adrenal tumours and registered between 2015 and 2020 were included and compared for morbidity, length of hospital stay, and conversion to open surgery.

Results A total of 2660 patients from 11 different countries and 69 different hospitals were analyzed and 1696 LTA were compared to 964 PRLA. Length of hospital stay was shorter after RPLA, with less patients ($N=434$, 45.5%, vs $N=1094$, 65.0%, $p<0.001$) staying more than 2 days. In total, 96 patients (3.6%) developed a complication Clavien-Dindo grade 2 or higher. No statistical difference was found between both study groups. After propensity score matching, length of hospital stay was shorter after PRLA (> 2 days 45.2% vs 63.0%, $p<0.001$). After multivariable logistic regression, factors associated with morbidity were age (OR 1.03), male sex (OR 1.52), and conversion to open surgery (OR 5.73).

Conclusion This study presents the largest retrospective observational analysis comparing LTA and PRLA. Our findings confirm the shorter length of hospital stay after PRLA. Both techniques are safe leading to comparable morbidity and conversion rates.

Keywords Adrenalectomy · Retroperitoneal · Laparoscopic · Morbidity · Length of hospital stay

Introduction

Laparoscopic transperitoneal adrenalectomy (LTA) is routinely performed to remove most adrenal tumours [1]. The keyhole approach has led to significant pain reduction, a shorter length of hospital stay, faster recovery, and better cosmetic results, without increasing morbidity or operating times compared to open surgery [2, 3]. Posterior retroperitoneal laparoscopic adrenalectomy (PRLA) was introduced as a feasible alternative to LTA with equal clinical outcomes [4–6]. Possible advantages of PRLA compared to LTA include less pain, shorter time to oral intake, even shorter length of hospital stay, less significant incisional hernias, and avoiding the intraperitoneal space [7–9].

A recent state-of-the-art meta-analysis comparing both minimal access techniques found significantly less estimated blood loss and length of hospital stay [4]. Remarkably, this

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difference was not seen in more recent studies. Only 12 randomized and non-randomized single-centre studies with small sample sizes in a high-volume tertiary setting could be included in an overall analysis of 775 patients. Categorization of studies according to surgical or institutional volume could not be performed and two separate time periods as surrogate for the learning curve had to be used instead.

The conflicting results from these small sample size studies merit further evaluation, as a potentially shorter hospital stay can reduce healthcare costs. Moreover, surgeon and institutional volume impact the outcome of endocrine surgery, including adrenalectomy, but minimum volume thresholds have not been set [10, 11].

This study aims to analyze PRLA versus LTA in adults using pan-European data comparing the largest number of patients to date, focusing on morbidity, length of hospital stay, and the influence of institutional volume on surgical outcome.

Material and methods

Study cohort

All adult patients that underwent PRLA or TLA between January 2015 and December 2020, registered in EUROCRINE®, were included in the analysis. Patients without histopathology results were excluded. Robot-assisted cases and bilateral adrenalectomies were excluded as they present subgroups with possible different advantages and morbidity, and as they were unequally divided amongst both study groups [12]. EUROCRINE® is an online, endocrine surgical quality registry that initially focused on rare endocrine tumours but has evolved into a pan-European database collecting data on all endocrine surgical procedures. It has already led to several papers in the field of adrenal surgery [12, 13]. Data entry is not mandatory, but EUROCRINE® board members are responsible for assessment of compliance on national level. Every participating centre has signed a specific agreement for correct data entry. Quality control happens at local, national, and international level. The study was approved by the EUROCRINE® board and by the institutional ethics review board of Ege University, Izmir (15e2/10). Neither financial support nor any free devices were received from the industry.

Patient characteristics and other variables

Basic patient characteristics (age, sex, body mass index (BMI, kg/m^2)) were collected. Preoperative characteristics included hormonal status (active, inactive), type of hormonal excess (aldosterone, cortisol, catecholamines, sex steroids), suspected malignancy on imaging and/or cytology, tumour side, and tumor size (mm). Operative characteristics included surgical technique, conversion to open surgery, and reasons for conversion. Conversion from either technique to open surgery was analyzed as "intention-to-treat". Surgical centres were classified as experienced if at least 36 adrenal surgical procedures were reported (6 cases per year for 6 years in a row), according to the European Society of Endocrine Surgeons (ESES) consensus guidelines [11]. Postoperative characteristics included length of hospital stay (defined as the number of days in hospital after surgery, dichotomized at a threshold of 2 days), 30-day morbidity, hospital readmission, and 30-day all-cause mortality. In view of the information provided from predefined and free text data fields, all complications were categorized according to the Clavien-Dindo classification [14]. Also, histopathological outcomes and completeness of resection were collected.

The primary outcome was morbidity (Clavien-Dindo score of 2 or more). The secondary outcomes were length of hospital stay and conversion to open surgery. Sensitivity analyses were performed for patients with tumour sizes > 50 mm, patients with BMI > 30 kg/m^2, patients with phaeochromocytoma, and according to side of the tumour as they present additional surgical and anatomical challenges. Threshold values were set based on previous studies [15–17].

Statistical analysis

The Shapiro–Wilk test was used to test normality of the numerical variables. Categorical continuous variables are reported as medians and interquartile ranges (IQR), and nominal variables as counts and percentages. Descriptive statistics were used to compare differences between patients that underwent PRLA and LTA, using the chi-square test, Fisher's exact test, and the Mann–Whitney *U* test, as appropriate.

To identify associations between morbidity with preoperative and postoperative variables, forward stepwise (likelihood ratio) logistic regression analysis was conducted. Variables with associations $p < 0.100$ in univariate analysis were included in multiple logistic regression model to generate odds ratios (OR). For the logistic model, OR, 95% confidence intervals (CI), and associated *p* values are reported.

Propensity score matching was used to account for possible confounders on outcome [18]. Propensity scores (ranging from 0 to 1, the probability of a patient assigned to PRLA or LTA) were derived using a logistic regression model including age, sex, BMI, tumour size, centre experience, and hormonal excess status. One-to-one propensity score matching was performed by nearest neighbour matching within a calliper of 0.2. The balance of confounding variables between both groups of the matched data was assessed with standardized mean differences (SMD). SMD < 10% is a recommended threshold for reporting balance [18]. All statistical analyses were conducted using IBM SPSS Statistics for Windows (version 25.0, Armonk, NY) and R 3.6.3 open-source software with "MatchIt" package (http://www.R-project.org).

Results

A total of 3780 patients were entered in the EUROCRINE® registry from 01/2015 to 12/2020, and 2660 patients from 11 different countries and 69 different hospitals met the criteria to be included in the study. Reasons for exclusion are summarized in Fig. 1. Of those, 1696 underwent an LTA (63.8%) and 964 a PRLA (36.2%). Patient, hospital, preoperative, and tumour characteristics are summarized in Table 1. In the overall cohort, median age was 54 (44–64) years, female-to-male was ratio 1.4, and median BMI was 27.2 (23.8–30.9) kg/m^2 with 777 patients (30%) being obese. PRLA was more frequently performed in experienced centres, in female, younger, heavier patients, and in right-sided tumours. Most tumours ($N=1671$, 62.8%) were hormonally active, with aldosterone ($N=767$, 28.8%) being the most frequent hormone. More phaeochromocytomas and less cortisol-secreting tumours were operated via LTA ($p<0.001$). Median tumour size was 33 (20–50) mm. In 844 patients (31.8%), a malignancy was suspected on imaging and/or cytology prior to surgery, whereas 206 patients (7.7%) underwent adrenal surgery for metastasis. Tumour size was the main indication for surgery in 283 patients (10.6%), with a median tumour size of 50 (40–63) mm in this subgroup. A conversion to open surgery was performed in 44 patients (1.7%), mainly because of bleeding ($N=20$), difficult access ($N=12$), unclear anatomy ($N=11$), or adhesions ($N=5$).

Surgical outcome, morbidity, and final histopathology are summarized in Table 2. In total, 96 patients (3.6%) developed a complication Clavien-Dindo grade 2 or higher. No statistical difference was found between both study groups. Most common complications were all-cause infections ($N=45$, 1.7%), respiratory complications ($N=18$, 0.7%), and haemorrhage requiring blood transfusion ($N=17$, 0.6%).

Length of hospital stay was longer in the LTA group, with more patients staying over 2 days ($N=1094$, 65.0% vs $N=434$, 45.5%, $p<0.001$). Thirteen patients (0.5%) were reoperated, and 40 patients (1.5%) had to be readmitted after discharge. The 30-day all-cause mortality was low ($N=4$, 0.2%). Final histopathology showed 60 adrenocortical cancers (2.3%), 1382 adrenocortical adenomas (52.0%), and 546 phaeochromocytomas (20.5%).

Factors associated with morbidity (Clavien-Dindo grade 2 or higher) after adrenalectomy in the univariate logistic regression analysis included age, male sex, conversion to open surgery, and centre inexperience. After multivariable

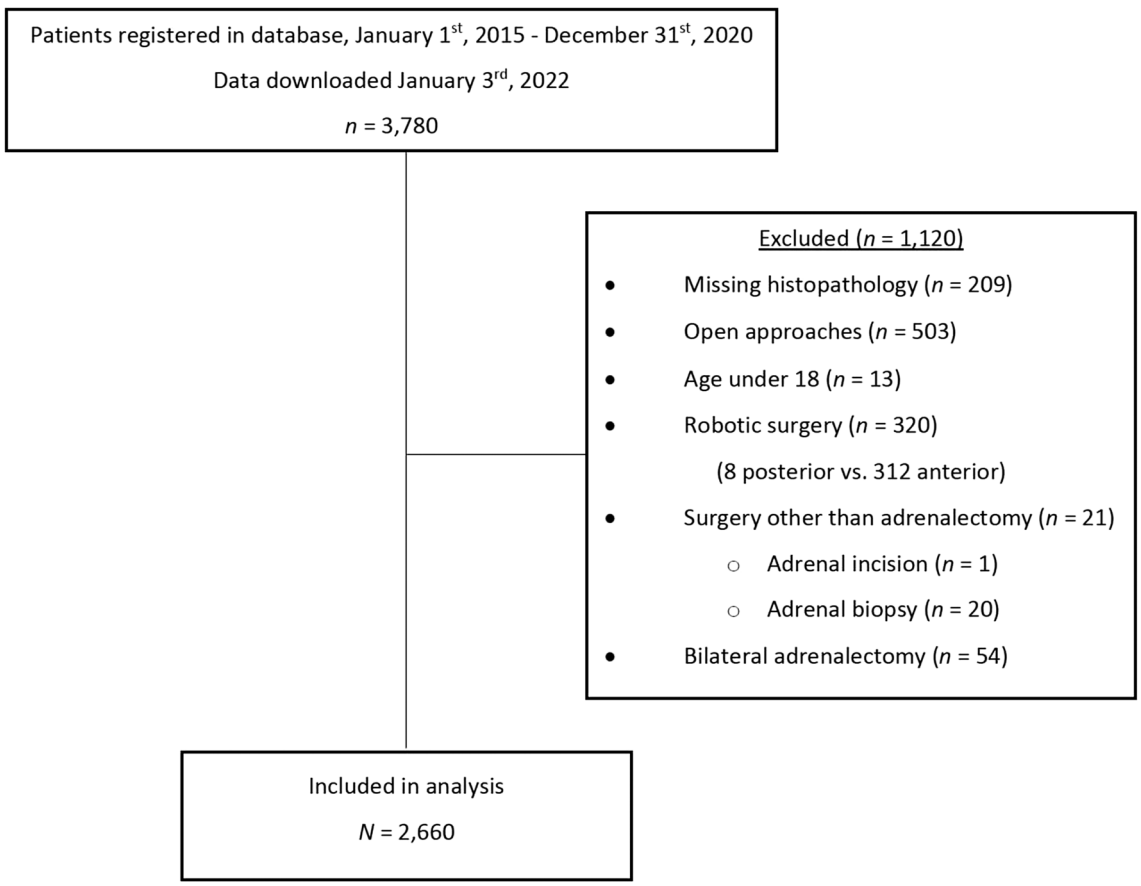

Fig. 1 Flowchart with reasons for exclusion

Table 1 Baseline preoperative characteristics, according to surgical technique

	Total ($N=2660$)	LTA ($N=1696$, 63.8%)	PRLA ($N=964$, 36.2%)	p value
Age, median (IQR), years	54 (44–64)	55 (44–64)	54 (43–62)	.003
Sex, *N* (%)				.003
Female	1554 (58.4)	955 (56.3)	599 (62.1)	
Male	1106 (41.6)	741 (43.7)	365 (37.9)	
BMI, median (IQR), kg/m^2	27.2 (23.8–30.9)	26.9 (23.6–30.4)	27.5 (24.2–31.6)	.001
<30, *N* (%)	1815 (70.0)	1182 (72.2)	633 (66.4)	.002
≥ 30, *N* (%)	777 (30.0)	456 (27.8)	321 (33.6)	
Centre experience, *N* (%)				.002
Experienced	2254 (84.7)	1409 (83.1)	845 (87.7)	
Inexperienced	406 (15.3)	287 (27.8)	119 (12.3)	
Diagnosis, *N* (%)				$<.001$
Incidental	1334 (50.2)	748 (44.2)	586 (60.8)	
Adrenal-related symptoms	1323 (49.8)	945 (55.8)	378 (39.2)	
Hormonal status, *N* (%)				.294
Active	1671 (62.8)	1078 (63.6)	593 (61.5)	
Inactive	989 (37.2)	618 (36.4)	371 (38.5)	
Hormonal excess, *N* (%)				$<.001$
Aldosterone	767 (28.8)	519 (30.6)	248 (25.7)	
Cortisol	393 (14.8)	222 (13.1)	171 (17.7)	
Catecholamines	514 (19.3)	339 (20.0)	175 (18.2)	
Sex steroids	11 (0.4)	9 (0.5)	2 (0.2)	
Indication for surgery, *N* (%)				
Suspected malignancy on imaging	824 (31.0)	411 (24.2)	413 (42.8)	$<.001$
Suspected malignancy on cytology	20 (0.8)	14 (0.8)	6 (0.6)	.560
Surgery for size	283 (10.6)	184 (10.8)	99 (10.3)	.641
Tumour size, median (IQR), mm	50 (40–63)	50 (40–70)	44.5 (30.5–59.5)	.001
Surgery for metastasis	206 (7.7)	134 (7.9)	72 (7.5)	.689
Tumour size, median (IQR), mm	33 (20–50)	33 (20–50)	35 (20–50)	.914
<50	1767 (72.2)	1113 (70.8)	654 (74.6)	.046
≥ 50	682 (27.8)	459 (29.2)	223 (25.4)	
Tumour side, *N* (%)				.039
Right	1237 (47.7)	762 (46.2)	475 (50.4)	
Left	1357 (52.3)	889 (53.8)	468 (49.6)	

IQR interquartile range, *LTA* laparoscopic transperitoneal adrenalectomy, *N* number, *PRLA* posterior retroperitoneal laparoscopic adrenalectomy

logistic regression analysis, age (OR 1.03, 95%CI 1.01–1.04, $p=0.002$), male sex (OR 1.52, 95%CI 1.01–2.29, $p=0$ 0.047), and conversion to open surgery (OR 5.73, 95%CI 2.57–12.79, $p<0.001$) were the only factors associated with morbidity (Clavien-Dindo grade 2 or higher) (Table 3).

Sensitivity analyses comparing LTA and PRLA showed a longer length of hospital stay after LTA in patients with BMI ≥ 30 kg/m^2 (63.7% vs 50.2%, $p<0.001$), with tumour size ≥ 50 mm (71.7% vs 47.7%, $p<0.001$), and with phaeochromocytoma (77.9% vs 60.3%, $p<0.001$). No differences in conversion rate were found in these subgroups (data not shown).

Sixty patients (39 LTA vs 21 PRLA) underwent surgery for adrenocortical cancer. PRLA was only performed in experienced centres (100%) in younger patients (44 vs 58 years old, $p<0.001$) without differences in length of hospital stay ($p=0.465$) or morbidity (Clavien-Dindo grade 2 or higher) ($p=0.537$). Remarkably, in 185 patients (121 LTA and 64 PRLA) undergoing surgery for malignant adrenal tumours (other than adrenocortical cancer and phaeochromocytomas), length of hospital stay was not statistically different ($p=0.307$), but morbidity (Clavien-Dindo grade 2 or higher) significantly higher after PRLA (15.6% vs 5.0%, $p=0.014$).

Subgroup analysis according to side of the tumour showed that patients with left-sided tumours were slightly younger (54 vs 55 years old, $p=0.047$), heavier (BMI ≥ 30 kg/m^2, 33.7% vs 28.0%, $p=0.030$), and operated more in experienced

Table 2 Outcomes, according to surgical technique

	Total ($N=2660$)	LTA ($N=1696$, 63.8%)	PRLA ($N=964$, 36.2%)	p value
Length of hospital stay, *N* (%), days				< .001
≤ 2	1108 (42.0)	589 (35.0)	519 (54.5)	
> 2	1528 (58.0)	1094 (65.0)	434 (45.5)	
Conversion to open surgery, *N* (%)	44 (1.7)	32 (1.9)	12 (1.2)	.212
Morbidity, *N* (%)	96 (3.6)	69 (4.1)	28 (2.9)	.133
Clavien-Dindo (dichotomized), *N* (%)				.728
Grade < 2	2164 (96.4)	1900 (95.9)	936 (97.1)	
Grade ≥ 2	96 (3.6)	69 (4.1)	28 (2.9)	
Reoperation, *N* (%)	13 (0.5)	9 (0.5)	4 (0.4)	.780
Wound infection, *N* (%)	32 (1.2)	23 (1.4)	9 (0.9)	.337
Hospital readmission, *N* (%)	40 (1.5)	29 (1.7)	11 (1.1)	.247
30-day mortality, *N* (%)	4 (0.2)	3 (0.2)	1 (0.1)	1.000
Histopathology, *N* (%)				.378
Adrenal cortical adenoma	1382 (52.0)	891 (52.5)	491 (50.9)	
Adrenal cortical cancer	60 (2.3)	39 (2.3)	21 (2.2)	
Phaeochromocytoma	546 (20.5)	354 (20.9)	192 (19.9)	
Other benign	487 (18.3)	291 (17.2)	196 (20.3)	
Other malignant	185 (7.0)	121 (7.1)	64 (6.6)	

LTA laparoscopic transperitoneal adrenalectomy, *N* number, *PRLA* posterior retroperitoneal laparoscopic adrenalectomy

centres (87.8% vs 83.3%, $p=0.008$) when operated via PRLA. Length of hospital stay was shorter (> 2 days, 41.6% vs 65.7%, $p<0.001$) and morbidity (Clavien-Dindo grade 2 or higher) lower in the PRLA group (2.1% vs 4.4%, $p=0.035$) (Supplementary Table S1). Patients with right-sided tumours were slightly younger (54 vs 55 years old, $p=0.010$) and heavier (BMI ≥ 30 kg/m^2, 33.6% vs 26.7%, $p=0.010$) with smaller tumour sizes (≥ 50 mm 26.2% vs 31.9%, $p=0.037$) when operated via PRLA. Length of hospital stay was shorter (> 2 days 47.4% vs 62.9%, $p<0.001$) (Supplementary Table S2).

After propensity score matching, 865 patients could be included in both groups. The predefined possible confounding variables (age, sex, BMI, centre experience, and hormonal status) were equally distributed (SMD < 10%) (Supplementary Table S3). Length of hospital stay was shorter after PRLA (> 2 days, 45.2% vs 63.0%, $p<0.001$). There was no significant difference between LTA and PRLA in terms of conversion rate, morbidity (Clavien-Dindo grade 2 or higher), wound infection, reoperation, or hospital readmission (Table 4).

Discussion

This European retrospective analysis of a prospective cohort compared 964 posterior retroperitoneal and 1696 transperitoneal laparoscopic adrenalectomies. Length of hospital stay was significantly shorter after PRLA. Overall morbidity (Clavien-Dindo grade 2 or higher) was low and comparable between both groups. Factors associated with morbidity after multivariable logistic regression included age, male sex, and conversion to open surgery. Sensitivity analysis for obesity (BMI ≥ 30 kg/m^2), tumour size (≥ 50 mm), and phaeochromocytoma confirmed the shorter length of hospital stay after PRLA. The statistical significance of the shorter length of hospital stay after PRLA remained after propensity score matching.

The significant reduction in length of hospital stay after PRLA compared to LTA was previously found in a recent state-of-the-art meta-analysis analyzing 775 patients from 3 randomized controlled and 9 non-randomized comparative trials [4]. Possible explanations are reduced insufflation pressures and avoiding a pneumoperitoneum in PRLA [8]. In addition, avoiding surgical access to the retroperitoneum via the lumbar region with less sensitive skin innervation, the use of only 3 ports, and avoiding intra-abdominal dissection also might result in faster postoperative recovery [8]. The previous doubts on PRLA in larger tumour sizes and male/female differences were not confirmed by our subgroup analyses. In our series, the side of the adrenalectomy was not a risk factor for morbidity (including postoperative bleeding) in contrast with the findings of a recent meta-analysis including 780 patients with LTA.

Surgical volume and institutional volume have proven to impact outcomes after adrenalectomy [19, 20]. Moreover, a recent multicentre study evaluated hemodynamic instability during surgery for phaeochromocytoma via LTA and PRLA and noticed a significant inter-centre effect [21]. The

Table 3 Univariate and multiple logistic regression analysis assessing risk for Clavien-Dindo grade ≥ 2

	Univariable logistic regression			Multivariable logistic regression		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Age	1.03	1.01–1.04	.001	1.03	1.01–1.04	.002
Sex						
Female	1			1		
Male	1.65	1.10–2.49	.015	1.52	1.01–2.29	.047
Conversion						
No	1			1		
Yes	6.31	2.85–13.97	< .001	5.73	2.57–12.79	< .001
Centre experience						
Experienced	1					
Inexperienced	1.67	1.02–2.71	.040			
Histopathology						
Other benign	1					
Other malignant	3.20	1.53–6.69	.002			
ACA	1.11	0.60–2.05	.735			
ACC	1.17	0.26–5.26	.842			
Phaeochromocytoma	1.35	0.68–2.69	.391			
BMI						
< 30 kg/m^2	1					
≥ 30 kg/m^2	1.25	0.82–1.93	.303			
Tumour side						
Left	1					
Right	1.01	.067–1.52	.971			
Tumour size						
< 50 mm	1					
≥ 50 mm	1.43	0.91–2.23	.118			
Hormonal status						
No	1					
Yes	0.80	0.53–1.21	.292			
Aldosterone excess						
No	1					
Yes	0.72	0.44–1.16	.175			
Catecholamines excess						
No	1					
Yes	1.16	0.71–1.90	.555			
Sex steroids excess						
No	1					
Yes	2.66	0.34–20.99	.353			
Cortisol excess						
No	1					
Yes	1.15	0.66–1.98	.627			
Surgical technique						
PRLA	1					
LTA	1.42	0.91–2.22	.125			

ACA adrenocortical adenoma, *ACC* adrenocortical cancer, *CI* confidence interval, *LTA* laparoscopic transperitoneal adrenalectomy, *OR* odds ratio, *PRLA* posterior retroperitoneal laparoscopic adrenalectomy

previously mentioned meta-analysis could only include single-centre studies from high-volume, tertiary endocrine surgery units [4]. After propensity score matching for centre experience in our European series, morbidity remained comparable, and length of hospital stay remained shorter. No modifiable risk factors for morbidity could be identified.

Table 4 Outcomes after propensity score matching, according to surgical technique

	LTA ($N=865$)	PRLA ($N=865$)	p value
Length of hospital stay, *N* (%), days			< .001
≤ 2	320 (37.0)	474 (54.8)	
> 2	545 (63.0)	391 (45.2)	
Conversion to open surgery, *N* (%)	7 (0.8)	9 (1.0)	.615
Clavien-Dindo (dichotomized), *N* (%)			.209
Grade ≥ 2	31 (3.6)	22 (2.5)	
Reoperation, *N* (%)	5 (0.6)	3 (0.3)	.726
Wound infection, *N* (%)	15 (1.7)	7 (0.8)	.086
Hospital readmission, *N* (%)	16 (1.8)	9 (1.0)	.158
30-day mortality, *N* (%)	1 (0.1)	1 (0.1)	1.000

LTA laparoscopic transperitoneal adrenalectomy, *N* number, *PRLA* posterior retroperitoneal laparoscopic adrenalectomy

In case of adrenalectomy for adrenal malignancies beyond phaeochromocytomas and adrenocortical cancers, no differences in length of hospital stay were found and significantly more morbidity after PRLA. This subgroup mainly includes surgery for adrenal metastases. To our knowledge, the increased morbidity after PRLA has not been previously reported and warrants further research.

To our knowledge, this is the largest, international, multicentre analyses of a recent surgical cohort based on a European quality registry. Data from high- and low-volume centres could be evaluated. Different subgroup analyses have confirmed the overall results.

Some limitations of this study are acknowledged. Data on specific surgeon experience within the high- and low-volume experienced centres is lacking. Length of hospital stay might be influenced by differences of healthcare reimbursement amongst the participating European countries. As other registries, EUROCRINE registry is prone to typing and coding errors, and missing data. No information on estimated blood loss, operative times, and healthcare costs was available. The type of complication data had been registered in the predefined and free text data fields for only 108 patients.

Both surgical techniques are feasible and safe and have a clear advantage on open surgery. The shorter length of hospital stay after PRLA is important as it can influence future healthcare and hospital ward planning, and it may subsequently reduce healthcare costs. However, prospective studies are necessary to confirm the health economic impact of a shorter length of hospital stay. Future studies should try to correct for surgeon experience, differences in operative times, and estimated blood loss.

Conclusion

This study presents the largest retrospective observational analysis comparing LTA and PRLA. Our findings confirm the shorter length of hospital stay after PRLA. Both techniques are safe leading to comparable morbidity and conversion rates.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00423-023-02975-5.

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Authors' contributions Drs S. Vatansever and Ö. Makay had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design: Drs K. Van Den Heede, S. Vatansever, and Ö. Makay.

Acquisition of data: Drs S. Vatansever and Ö. Makay.

Analysis and interpretation of data: All authors.

Drafting of manuscript: Dr K. Van Den Heede.

Critical revision of the manuscript: All authors.

Data availability The data that support the findings of this study are available from the corresponding author, KV, upon reasonable request.

Declarations

Competing interests The authors declare no competing interests.

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