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Laparoscopic transperitoneal adrenalectomy: a comparative study of different techniques for vessel sealing

Luca Cardinali[1] · Edlira Skrami[2] · Elisa Catani[1] · Flavia Carle[2] · Monica Ortenzi[1] · Andrea Balla[3] · Mario Guerrieri[1]

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Abstract

Background Laparoscopic adrenalectomy is the standard surgical approach to adrenal lesions. Adrenal vessel sealing is the critical surgical phase of laparoscopic adrenalectomy. This study aimed at comparing perioperative outcomes of laparoscopic transperitoneal adrenalectomy by means of radiofrequency energy-based device (LARFD) to those performed with traditional clipping device (LACD), while focusing on the different adrenal vessel control techniques.

Methods Patients who underwent adrenalectomy for adrenal disease between January 1994 and April 2019 at the Surgical Clinic, Polytechnic University of Marche were included in the study. Overall, 414 patients met inclusion criteria for study eligibility: 211 and 203 patients underwent LARFD and LACD, respectively. Multiple models of quantile regression, logistic regression and Poisson finite mixture regression were used to assess the relationship between operative time, conversion to open procedure, length of stay (LoS), surgical procedure and patient characteristics, respectively.

Results LARFD reduced operative time of about 12 min compared to LACD. Additional operative time-related factors were surgery side, surgery approach, conversion to open procedure and trocar number. The probability of conversion to open procedure decreased by about 76% for each added trocar, whereas it increased by about 49% for each added centimeter of adrenal lesion and by about 25% for each added year of surgery. Two patient clusters were identified based on the LoS: long-stay and short-stay. In the long-stay cluster, LoS decreased of about 30% in LARFD group and it was significantly associated with conversion to open procedure and postoperative complications, whereas in short-stay cluster only postoperative complications had a significant effect on LoS.

Conclusion Laparoscopic transperitoneal adrenalectomy performed by means of radiofrequency energy-based device for the sealing of adrenal vessels is an effective procedure reducing operative time with potentially improved postoperative outcomes.

Keywords Laparoscopic adrenalectomy · Minimally invasive surgery · Radiofrequency · Vessel sealing · Adrenal gland

Laparoscopic adrenalectomy was successfully performed and described for the first time by Gagner in 1992 [1]. Since then, laparoscopic adrenalectomy has been gaining worldwide while being mentioned by an increasing number of reports in the literature [2–5]. Nowadays, laparoscopic adrenalectomy is universally acknowledged as the gold standard for the treatment of adrenal diseases [6]. Benefits of laparoscopic adrenalectomy over the open approach, such as lesser postoperative pain, reduced blood loss, more rapid bowel function, shorter hospital stay, enhanced cosmetic outcome and earlier return to daily activities, have been widely reported by several studies [4, 7, 8].

Over time, the worldwide spread of laparoscopic surgery acted as a forerunner for new technologies and fostered the development of advanced devices, including various energy tools for the sealing, coagulating and cutting of blood vessels. Vascular control and dissection maneuvers, among the other things, play a key role in reducing operative bleeding and intra-/postoperative complications.

✉ Luca Cardinali
cardinali.luca@hotmail.it

[1] Surgical Clinic, Department of Experimental and Clinical Medicine, Section of Surgical Sciences, Polytechnic University of Marche, Via Tronto 10/A, 60126 Ancona, Italy

[2] Centre of Epidemiology, Biostatistics and Information Technology, School of Medicine, Polytechnic University of Marche, Ancona, Italy

[3] Department of General Surgery and Surgical Specialties "Paride Stefanini", Sapienza University of Rome, Rome, Italy

The aim of this study is to compare perioperative and short-term outcomes of laparoscopic transperitoneal adrenalectomy by means of radiofrequency energy-based device (LARFD) to those performed with traditional clipping device (LACD) while focusing on the different adrenal vessel-sealing techniques.

Patients and methods

Patients

A historical prospective study on patients undergoing laparoscopic adrenalectomy for adrenal diseases from January 1994 to April 2019 at the Surgical Clinic of the Department of Experimental and Clinical Medicine, Polytechnic University of Marche, was carried out during May–July 2019. Figure 1 shows the study flow chart (Fig. 1). During this period, 447 laparoscopic transperitoneal adrenalectomies were performed. Patients who underwent laparoscopic bilateral adrenalectomy, concomitant surgical procedures besides laparoscopic adrenalectomy and those who underwent laparoscopic adrenalectomy performed without radiofrequency energy-based device for the gland dissection were excluded.

Overall, 414 patients met inclusion criteria for study eligibility. Therefore, 211 patients who underwent laparoscopic transperitoneal adrenalectomy via radiofrequency energy-based device (LARFD) for vessel sealing were analyzed and their results subsequently compared with those of 203 patients who underwent laparoscopic transperitoneal adrenalectomy with traditional vessel clipping (LACD).

Patient allocation in one of the two groups was decided on surgery day based on preoperative availability of the same radiofrequency device model used to perform vascular surgical time: if it was available, patient was allocated to LARFD group; otherwise, the surgeon performed adrenal vessel sealing via traditional clipping device and patient was therefore allocated to LACD group. All procedures were performed by two surgeons (GM, CR) with high-level experience in conventional abdominal laparoscopy.

Institutional review board approval and informed consent from participants are no need for this study.

Perioperative management

Perioperative management was standardized for all patients. Preoperative diagnosis was performed by clinical, biochemical and imaging examinations including abdominal ultrasonography (US), computed tomography (CT) scan, and/or magnetic resonance (MR) imaging. Biochemical evaluation for excessive hormonal levels (hypersecretion of glucocorticoid, mineralocorticoid, sex steroids, and catecholamines) was based on the evaluation of basal and dynamic hormonal tests.

A contrast CT scan or RM imaging was performed in all patients. If CT findings suggested adrenal adenoma or mesenchymal benign tumor, additional imaging tests were not recommended; otherwise, if clinical and biochemical evaluation revealed abnormal increase in steroid metabolites such as dehydroepiandrosterone sulfate (DHEA-S), or imaging showed findings suspect for malignant adrenal tumor such as diameter ≥ 4 cm, irregular margins, inhomogeneous contrast enhancement, presence of surrounding tissue

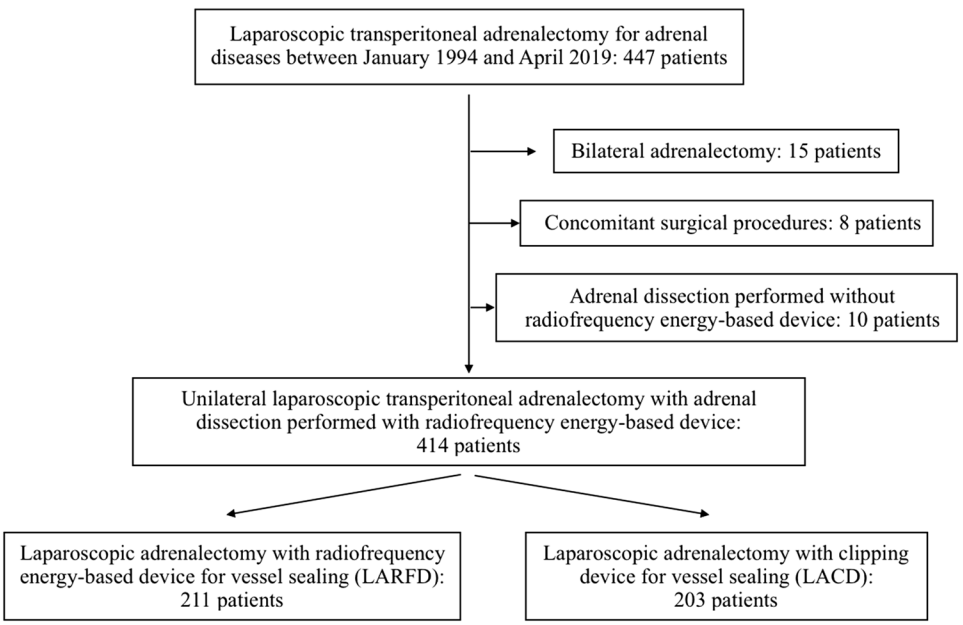

Fig. 1 Study flow chart

invasion or metastasis, Hounsfield unit (HU) value higher on a non-contrast CT scan (≥ 10 HU) and contrast washout rate lower in the delayed view of a contrast CT scan (absolute washout < 60%, relative washout < 40%), a 18F-FDG-PET/CT was considered as additional diagnostic method [9].

When pheochromocytoma was suspected or could not be completely ruled out, α-blocker therapy for 7–14 days prior to surgery was administered to prevent cardiovascular complications.

Oral feeding was started at first postoperative day and patients were discharged once they were free from any complications.

Demographic and clinical patient characteristics (gender, age, body mass index [BMI], medical comorbidities, history of previous malignancy and laparotomy) were recorded at patient hospitalization; adrenal mass characteristics (clinical presentation, type of produced hormone, preoperative diagnosis and adrenal size based on CT scan) and surgical procedure characteristics (laterality, surgical approach and number of trocars used) were recorded after surgery. All patients were followed for at least 30 days after surgery.

Operative data, including operative time, conversion to open procedure, operative and postoperative complications, bleeding rate demanding blood transfusions, reoperation, length of stay (LoS), readmission and hospital mortality were recorded. Operative time was calculated from skin incision to skin closure. Hospital mortality was defined as overall in-hospital deaths and deaths occurring within 30 days as of discharge unless clearly unrelated to the procedure. All patients were assessed for both postoperative complications (between surgery day and discharge) and post-discharge complications requiring readmission (between discharge and two outpatient consultations on day 7 and 30 as of surgery). Postoperative complications were recorded and graded according to the "Extended Clavien-Dindo (ECD) Classification of Surgical Complications" [10]. Infected lymphocele was defined as a clinically relevant condition characterized by lymph fluid output of any measurable volume via abdominal drain with milky-white appearance and high levels of triglycerides. Abdominal or retroperitoneal abscess was defined as an intra-abdominal or retroperitoneal collection of purulent or infected material, clinically and radiologically highlighted, that required antibiotic therapy and drainage.

Surgical techniques

Surgical approach by submesocolic and anterior transperitoneal route as well as related technical details have been previously described [11–14].

In LARFD group, adrenal vessels were sealed and cut by exclusively using a radiofrequency energy-based device: vascular control was ensured by one or two consecutive and adjacent applications of current, after which vessels were divided leaving at least 3–5 mm length of fused tissue on the patient side. On the other hand, in LACD group adrenal vessels were traditionally divided between non-absorbable clips.

Statistical analysis

The Shapiro–Wilk test was used to evaluate variable distribution. Variables were not found to be normally distributed; therefore, a non-parametric approach was used to statistical analysis.

Quantitative variables were summarized using median and interquartile range (1st–3rd quartile), qualitative variables as absolute and percentage frequencies. Comparisons between the two groups were performed by means of the Wilcoxon–Mann–Whitney test for quantitative variables, and Chi-square test or Fisher test (when expected frequencies were lower than 5) for qualitative variables. The Benjamini and Hochberg correction was applied to adjust *p*-values for multiple testing on the same data set.

A multiple quantile regression [15] analysis was performed to evaluate operative time-related factors (dependent variable). Quantile regression does not hold any assumption on the variable distribution and it allows estimating the effect of independent variables on the quantile distribution of dependent variable. In this analysis, the dependent variable median was evaluated; the surgery type was the independent variable, and patient's before-surgery and surgery-related characteristics were the covariates. Quantile regression analysis results were expressed as point and interval estimates of regression coefficients. When the 95% Confidence Intervals (CIs) did not include 0, regression coefficients were considered statistically significant. The final model was the most parsimonious one, including the covariates that most contributed to the goodness of fit.

Multiple logistic regression analysis was used to assess the role of surgical approach, patient characteristics and surgical characteristics on the likelihood of conversion to open procedure. All estimates were evaluated by means of 95% CIs. Likelihood ratio (LR) test and Hosmer–Lemeshow (HL) test were used to select the most parsimonious model and to evaluate the model's goodness of fit.

The inpatient LoS was analyzed using a Poisson finite mixture regression model [16]. This type of analysis is suitable to positively skewed model, over-dispersed distributions of count data and is able to account for unobserved heterogeneity that clusters around a finite set of subgroups with different patterns. A two-component finite mixture Poisson model was chosen by comparing the fit of models with different number of components through the Akaike Information Criteria (AIC). The two components were classified into short- and long-stay groups. In the model, type of surgery,

laterality, postoperative complications, age classes and surgery period were considered as covariates, as well as those that most contributed to the goodness of fit.

A level of probability lower than 0.05 was established to assess statistical significance. The statistical analyses were performed using R version 3.5.3 [17].

Results

Patient characteristics

Demographic and clinical characteristics of the patients according to surgery type (LARFD vs. LACD) were summarized in Table 1. There were statistically significant differences between the two groups in terms of median age ($p = 0.004$) and obesity comorbidity ($p = 0.015$): patients who underwent LARFD were older and more obese than those of LACD group.

Surgical procedure characteristics

Between January 1994 and December 2003, LACD procedure was the only one performed in the considered Surgical Clinic. As of January 2004, both procedures were available and LARFD was used more frequently with respect to LACD (53 and 211 subjects, respectively).

The distribution of surgery-related characteristics according to surgery type is shown in Table 2. LACD was more frequently performed in anterior and flank approaches, whereas submesocolic approach was the one most frequently carried out in LARFD group. Moreover, the median number of trocars used during surgery was significantly higher in LARFD group.

Operative and postoperative outcomes

Operative and postoperative outcomes are reported in Table 3. Median operative time was 65 (1st; 3rd quartiles: 52.5; 85) minutes and 100 (1st; 3rd quartiles: 80; 135) minutes in LARFD and LACD groups, respectively, whereas LoS was equal to 3 (1st; 3rd quartiles: 2.5; 4) days and 4 (1st; 3rd quartiles: 3; 5) days in patients who underwent LARFD and LACD, respectively. While median operative time and median LoS were significantly lower in patients who underwent LARFD compared to those of LACD group, no significant differences between the two groups were found in terms of conversion to open procedure, operative and postoperative complications, bleeding and packed red blood cells transfused, reoperation, readmission, and hospital mortality.

Table 4 showed the postoperative complications graded according to ECD classification (Table 4). No differences between the two groups were reported regarding the severity of postoperative complications.

Pathological outcomes

Histological diagnosis and the size of both adenoma and adrenal gland were reported in Table 5. Median adrenal gland size and adenoma size were equal to 6 (1st; 3rd quartiles: 5; 6.5) cm and 3 (1st; 3rd quartiles: 2; 4) cm in LARFD group and 6 (1st; 3rd quartiles: 5; 6.5) cm and 3 (1st; 3rd quartiles: 2; 4.5) cm in LACD group, respectively. No differences between the two groups were reported regarding pathological diagnosis and the size of adenoma and adrenal gland.

Factors associated to operative time

The results of multiple quantile regression are shown in Table 6. A lower operative time was significantly associated with LARFD compared to LACD (about 12 min less in median), to the right side of surgery compared to the left side (about 20 min less in median), to submesocolic approach compared to the anterior one (18 min less in median), and to the year of surgery (about 3 min less in median for each added year). Moreover, a higher operative time was significantly associated with the conversion to open procedure (about 47 min in median more than no conversion to open procedures) and to trocar number (about 47 min in median for each added trocar).

Factors associated to conversion to open procedure

Table 7 showed factors associated to the conversion to open procedure as a result from logistic regression (Table 7). Conversion to open procedure was significantly associated with number of trocars, adenoma size and year of surgery. In particular, likelihood of conversion to open procedure decreased by about 76% for each added trocar, increased by about 49% for each added centimeter of adenoma and by about 25% for each added year of surgery.

Factors associated to LoS

The two-component Poisson finite mixture regression model used to assess LoS had 27 observations under cluster 1 with a probability of 0.069 that were most likely those with a *long stay,* and 371 observations in cluster 2 with a probability of 0.931 that were most likely those with a *short stay*. The results of Poisson Mixture regression analysis are summarized in Table 8. Different LoS-related factors were identified for each cluster. In the *long-stay* cluster (component 1), type of surgery, conversion to open procedure and postoperative complications were significantly associated with LoS.

Table 1 Patient demographics and clinical characteristics according to the type of surgery

	LARFD ($n=211$)		LACD ($n=203$)		p
Gender[a]					
Male	82	(38.9)	76	(37.4)	1*
Female	129	(61.1)	127	(62.6)	
Age (years)[b]	58	(46.5; 65.8)	51.6	(41.3; 60.6)	0.004§
BMI (Kg/m^2)[b]	26.5	(24; 29.7)	26	(24; 29)	0.519§
Comorbidity[a]					
Hight blood pressure	114	(54)	97	(47.8)	0.519*
Cardiovascular disease	9	(4.3)	5	(2.5)	0.733*
Chronic obstructive pulmonary disease	1	(0.5)	3	(1.5)	0.613°
Chronic kidney disease	3	(1.4)	2	(1)	1°
Chronic liver disease	0	(0)	3	(1.5)	0.416°
Diabetes mellitus	17	(8.1)	7	(3.4)	0.230°
Obesity	47	(22.3)	22	(10.8)	0.015*
History of malignancy[a]	21	(10)	13	(6.4)	0.519*
History of laparotomy[a]	66	(31.3)	58	(28.6)	0.899*
Presentation[a]					
Incidental	96	(45.5)	84	(41.4)	0.433°
Arterial hypertension	86	(40.8)	86	(42.4)	
Cushing-Syndrome	29	(13.7)	28	(13.8)	
Virilizing Syndrome	0	(0)	5	(2.5)	
Functioning[a]					
Aldosterone	48	(22.7)	52	(25.6)	0.519°
Catecholamine	38	(18)	34	(16.7)	
Cortisol	30	(14.2)	28	(13.8)	
DHEA	0	(0)	4	(2)	
Cortisol–Aldosterone	2	(0.9)	0	(0)	
Cortisol–DHEA	0	(0)	1	(0.5)	
No	93	(44.1)	84	(41.4)	
Preoperative diagnosis[a]					
Incidentaloma	87	(41.2)	75	(36.9)	0.519°
Pheochromocytoma	38	(18)	34	(16.7)	
Conn-Syndrome	49	(23.2)	52	(25.6)	
Primary Cushing-Syndrome	30	(14.2)	28	(13.8)	
Virilizing Syndrome	0	(0)	5	(2.5)	
Metastasis	7	(3.3)	9	(4.4)	
Adrenal size on CT scan (cm)[b]	4.0	(2.7; 5.2)	3.3	(2.2; 4.7)	0.085§

LARFD laparoscopic adrenalectomy with radiofrequency energy-based device, *LACD* laparoscopic adrenalectomy with clip device, BMI body mass index, *DHEA* dehydroepiandrosterone, *CT* computer tomography

*Chi-square test

§Wilcoxon–Mann–Whitney test

°Fisher's exact test

[a]Qualitative variables are presented as absolute frequencies and percentages in brackets

[b]Quantitative variables are expressed as median and interquartile range (1st; 3rd quartile) in brackets

LoS decreased by about 30% in LARFD compared to LACD procedure, whereas it was 1.7 times higher in patients with conversion to open procedure compared to those with no conversion to open procedure. In addition, both abdominal and non-abdominal postoperative complications increased LoS compared to those with no postoperative complications in about three times and more than two times, respectively. Postoperative complications were the only factor that significantly influenced LoS in *short-stay* patients (component 2). LoS was 1.6 and 1.5 times higher with the occurrence

Table 2 Surgical procedure characteristics according to the type of surgery

	LARFD ($n=211$)		LACD ($n=203$)		p
Laterality[a]					
Left	100	(47.4)	97	(47.8)	1.000*
Right	111	(52.6)	106	(52.2)	
Surgical approach[a]					
Left adrenalectomy					
Anterior	24	(24.0)	66	(68.0)	< 0.001°
Submesocolic	74	(74.0)	16	(16.5)	
Flank	2	(2.0)	15	(15.5)	
Right adrenalectomy					
Anterior	111	(100)	97	(91.5)	0.001°
Flank	0	(0)	9	(8.5)	
Number of trocar[b]	5	(4; 5)	4	(4; 5)	< 0.001§

LARFD laparoscopic adrenalectomy with radiofrequency energy-based device, *LACD* laparoscopic adrenalectomy with clip device

*Chi-square test

§Wilcoxon–Mann–Whitney test

°Fisher's exact test

[a]Qualitative variables are presented as absolute frequencies and percentages in brackets

[b]Quantitative variables are expressed as median and interquartile range (1st; 3rd quartile) in brackets

of abdominal complications and non-abdominal complication, respectively, compared to patients with no postoperative complications.

Discussion

Nowadays, laparoscopic adrenalectomy is acknowledged as the gold standard treatment for adrenal diseases [6]. Several endoscopic approaches have been proposed for the management of adrenal gland lesions [13]. However, even if each author advocates the benefits inherent to their own approach, to date there is no evidence in literature supporting the superiority of an access over the other [2, 18]. Therefore, the most suitable approach—that is, a tailored approach based on patient and lesion features—is still open to debate [19]. As a consequence, and based on our experience with laparoscopic abdominal surgery and the submesocolic access to left adrenalectomy, the transperitoneal anterior approach is the most frequently mentioned one in this study.

Given that hemorrhage is one of the most frequent complications during surgery, an accurate hemostasis technique is even more important during laparoscopic surgeries, where a clean operating field is mandatory to reduce operative and postoperative complications. This issue is crucial in surgical procedures such as laparoscopic adrenalectomy, where operating field is narrow and close to major vessels [3]. The end arterial vessels of adrenal gland are generally small (< 3 mm) and easily managed by any coagulation devices; conversely, adrenal venous drainage runs through a single, large hilar vein (5 mm wide) whose control is vital for the successful outcome of surgical procedure [20]. The identification and dissection of adrenal vessels could sometimes be difficult due to patient obesity or to the extension of adrenal lesion behind the inferior cava vein in right adrenalectomy, or because it could closely adhere to the surrounding structures in the left one [14]. Assalia and Gagner reported the injury of main venous vessels (adrenal vein, renal vein and inferior cava vein) as the most frequent intraoperative complication, and bleeding as the most common postoperative complication [21, 22].

Different hemostatic techniques and devices have been developed over time, including laparoscopic suture ligation with different knots and knot applicators, the application of clips, staplers and various electrothermal and ultrasonic coagulation devices [23]. As previously reported by Harold et al., clip application is easy to perform but it requires an accurate vessel dissection with the risk of bleeding due to possible dislodgment during surgical maneuvers [24]. Therefore, in the last decades sophisticated energy-based dissection and hemostasis devices have been developed to facilitate complex laparoscopic procedures as laparoscopic adrenalectomy in which precision and thoroughness are of paramount importance [25]. The radiofrequency energy-based device, the most frequently used one in our clinical practice, is based on a technology that combines a precise amount of bipolar electrocoagulation (high current, low voltage) and pressure on the tissue leading to the denaturation of collagen and elastin in vessel walls and their fusion into a hemostatic seal [22, 23]. Moreover, by means of a tissue-based feedback mechanism to adjust the dosage of applied energy, this device allows to reduce local tissue damage compared to the traditional bipolar device [26].

The aim of the current study was to investigate the short-term outcomes of laparoscopic transperitoneal adrenalectomies with radiofrequency energy-based device (LARFD) compared to those performed by means of traditional clipping (LACD) for adrenal vessel control. While blunt dissection around the adrenal gland and coagulation of minor adrenal vessels was carried out via radiofrequency device in both groups, the division of adrenal vessels was performed entirely with a radiofrequency energy device in LARFD group only. On the other hand, in LACD group adrenal vessels were sectioned after the application of dual titanium clips. The literature reports only two case series evaluating the hemostatic efficacy of radiofrequency system for the sealing of adrenal vessels during laparoscopic adrenalectomy [20, 27]. Therefore, to the best of our knowledge, this one is the study with the largest sample size comparing

Table 3 Operative and postoperative outcomes according to the type of surgery

	LARFD ($n=211$)		LACD ($n=203$)		p
Operative time (min)[b]	65	(52.5; 85)	100	(80; 135)	$<0.001^{\S}$
Conversion to open procedure[a]					
No	200	(94.8)	198	(97.5)	0.519*
Yes	11	(5.2)	5	(2.5)	
Operative complications[a]					
No	208	(98.6)	201	(99)	1.000°
Hemoperitoneum	3	(1.4)	1	(0.5)	
Pneumothorax	0		1	(0.5)	
Postoperative complications[a]					
No	194	(91.9)	190	(93.6)	0.899*
Abdominal complications	10	(4.7)	9	(4.4)	
Non-abdominal complications	7	(3.3)	4	(2)	
Bleeding[a]					
No	205	(97.2)	198	(97.5)	1.000*
Yes	6	(2.8)	5	(2.5)	
Blood transfusion[a]					
No	206	(97.6)	198	(97.5)	1.000*
Yes	5	(2.4)	5	(2.5)	
Packed red blood cells[b]	2	(1; 2)	2	(1; 2.5)	$0.833^{\S}$
Reoperation[a]					
No	211	(100)	201	(99)	0.519°
Yes	0		2	(1)	
Length of stay (LoS) (days)[b]	3	(2.5; 4)	4	(3; 5)	$0.008^{\S}$
Readmission[a]					
No	209	(99.1)	202	(99.5)	1.000°
Yes	2	(0.9)	1	(0.5)	
Hospital mortality[a]					
No	211	(100)	202	(99.5)	0.747°
Yes	0		1	(0.5)	

LARFD laparoscopic adrenalectomy with radiofrequency energy-based device, *LACD* laparoscopic adrenalectomy with clip device

*Chi-square test

§Wilcoxon–Mann–Whitney test

°Fisher's exact test

[a]Qualitative variables are presented as absolute frequencies and percentages in brackets

[b]Quantitative variables are expressed as median and interquartile range (1st; 3rd quartile) in brackets

these two different vessel-sealing techniques in laparoscopic transperitoneal adrenalectomy.

This study showed that LARFD and LACD had comparable surgical outcomes, operative and postoperative complications, conversion rate, transfusion rate, reoperation and readmission. According to the "Extended Clavien-Dindo Classification of Surgical Complications" [10], in our study the grade of postoperative complication was similar between the two groups. Only one case of exitus (ECD complication: grade V) was reported in LACD group due to bowel obstruction sequelae. As for operative and postoperative bleeding as well as the rate of anemia requiring transfusion—the most significant complications considered in this study to evaluate the sealing of the adrenal vessels by radiofrequency device—no difference between the two groups was reported. In this regard, the authors pointed out that the two groups were comparable in terms of both size and type of adrenal lesion removed. Furthermore, it was emphasized that even if patients in LARFD group were significantly older and mostly more obese than those in LACD group, the rate of operative and postoperative bleeding was similar in both groups.

An important aspect associated to the use of the radiofrequency energy-based device was the improved operative time. Multiple quantile regression analysis showed that operative time was significantly associated with the type of

Table 4 Postoperative abdominal and non-abdominal complications of LARFD and LACD patients according to the ECD classification

	LARFD		LACD		*p*
Abdominal complications[a]					
Grade I					0.425°
Wound infection	4	(40.0)	1	(11.10)	
Grade II					
Anemia requiring transfusion	5	(50.0)	4	(55.60)	
Grade IIIa					
Intrabdominal abscesses	0		1	(11.10)	
Infected lymphocele	1	(10.0)	0		
Grade IIIb					
Hemoperitoneum	0		1	(11.10)	
Colic fistula	0		1	(11.10)	
Grade V					
Bowel obstruction	0		1	(11.10)	
Total	10		9		
Non-abdominal complications[a]					
Grade I					0.546°
Urinary retension	3	(42.90)	3	(75.00)	
Grade II					
Supraventricular arrhythmia	1	(14.30)	0		
Pleural effusion	0		1	(25.00)	
Pneumonia	3	(42.90)	0		
Total	7		4		

LARFD laparoscopic adrenalectomy with radiofrequency energy-based device, *LACD* laparoscopic adrenalectomy with clip device, *ECD* extended Clavien-Dindo classification of surgical complications

[a]Qualitative variables are presented as absolute frequencies and percentages in brackets

°Fisher exact test

Table 5 Pathological characteristics according to the type of surgery

	LARFD (*n* = 211)		LACD (*n* = 203)		*p*
Histological diagnosis[a]					
Adenoma	99	(46.92)	105	(51.72)	0.519§
Myelolipoma	18	(8.53)	7	(3.45)	
Angioma	1	(0.47)	0		
Angiomyolipoma	1	(0.47)	0		
Carcinoma	6	(2.84)	4	(1.97)	
Cyst	4	(1.90)	3	(1.48)	
Pheochromocytoma	40	(18.96)	34	(16.75)	
Ganglioneuroma	1	(0.47)	2	(0.99)	
Oncocytoma	4	(1.90)	1	(0.49)	
Metastasis	7	(3.32)	10	(4.93)	
Hyperplasia	29	(13.74)	37	(18.23)	
Inflammatory mass	1	(0.47)	0		
Adrenal gland size (cm)[b]	6	(5; 6.5)	6	(5; 6.5)	1.000°
Adenoma size (cm)[b]	3	(2; 4)	3	(2; 4.5)	1.000°

LARFD laparoscopic adrenalectomy with radiofrequency energy-based device, *LACD* laparoscopic adrenalectomy with clip device

§Fisher's exact test

°Wilcoxon–Mann–Whitney test

[a]Qualitative variables are presented as absolute frequencies and percentages in brackets

[b]Quantitative variables are expressed as median and interquartile range (1st; 3rd quartile) in brackets

surgery (LARFD vs LACD), side (right vs. left), conversion to open procedure, surgical approach (submesocolic vs. anterior) and year of surgery. The use of the radiofrequency energy-based tool for the sealing of adrenal vessels reduced the operative time by about 12 min compared to traditional clipping. As previously assumed by Harold et al. the authors ascribed this result both to the extra-time needed to isolate the main adrenal vessels for clip placement and to the faster and safer vessel dissection as well as the higher hemostasis allowed by the use of radiofrequency energy-based device [24]. In addition, the greater manageability of the radiofrequency instrument allowing for synchronous vessel coagulation and separation ruled out the need to constantly change instruments thus reducing operative time [20]. Regression analysis showed that right-side procedure was found to be an independent predictor of decreased operative time. Indeed, median operative time was about 20 min longer in left adrenalectomy compared to the right one. This difference in operative time between left- and right-side adrenalectomy was similar to the one previously reported by other authors [5, 28]. The more necessary mobilization of splenic flexure, the close proximity of the left adrenal to pancreas tail and spleen, as well as the dissection of the left renal hilum to ensure vascular control of the left adrenal vein may be invoked as explanations for the increased time required to perform left-side adrenalectomy. More interestingly, the submesocolic approach proved to be a predictor of shorter procedure in left-side adrenalectomy. In the current experience, the median operative time in submesocolic route was about 18 min lower than the anterior route one. As previously stated [13, 19], the submesocolic approach allowed for both preliminary closure of adrenal vein, thus reducing intraoperative complications such as bleeding, and the overall fewer dissection maneuvers with minimal gland manipulation. These benefits could account for the lower operative time reported in submesocolic approach compared to the anterior one. A statistically significant association between operative time and year of surgery was reported. Median operative time was about 3 min shorter for each added year. In our opinion, this result could be explained by the greater experience acquired by the surgeon in carrying out a complex surgical procedure such as laparoscopic adrenalectomy.

Moreover, we found that the conversion rate to open procedure was significantly associated with the adenoma size and the number of trocars used. In particular, the likelihood

Table 6 Factors associated to the operative time: results of the quantile regression analysis

Variables	Modality	Regression coefficient	95% CI
Surgery type	LARFD vs LACD	−12.27	−26.22; −4.74
Laterality	Right vs Left	−21.05	−31.39; −6.57
Conversion to open procedure	Yes vs No	46.76	28.39; 81.26
Surgery approach	Flank vs Anterior	14.93	−1.05; 48.00
	Submesocolic vs Anterior	−18.21	−29.76; −6.66
Trocar	Number	13.73	7.53; 26.72
Size of surrenal	Centimeters	−0.16	−3.45; 3.26
Year of surgery	Years	−3.25	−4.06; −2.22
Age	Years	0.18	−0.03; 0.43

LARFD laparoscopic adrenalectomy with radiofrequency energy-based device, *LACD* laparoscopic adrenalectomy with clip device, 95% CI 95% Confidence Intervals

Table 7 Factors associated to the conversion to open procedure: results of the logistic regression analysis

Variables	Modality	OR	95% CI
Surgery type	LARFD vs LACD	0.63	0.17; 2.49
Laterality	Right vs Left	1.57	0.42; 6.70
Trocar	Number	0.24	0.07; 0.82
Adenoma size	Centimeters	1.49	1.07; 2.11
Year of surgery	Years	1.25	1.10; 1.47
Age	Years	1.02	0.98; 1.07

Hosmer and Lemeshow goodness of fit test: Chi-squared with 8 df, $\chi^2 = 3.57$, $p = 0.089$

LR test: Chi-squared with 6 df, $\chi^2 = 25.3$, $p = 0.002$

LARFD laparoscopic adrenalectomy with radiofrequency energy-based device, *LACD* laparoscopic adrenalectomy with clip device, *OR* odds ratio, *95% CI* 95% confidence intervals

of conversion to open procedure increased by about 49% for each added centimeter of adrenal lesion, while it decreased by about 76% for each added trocar. Historically, using laparoscopy for the treatment of adrenal lesions larger than 6 cm had been a topic of debate in the literature [2]. Despite the skepticism of some, other authors such as Gagner et al. who reported a radical adrenalectomy for a 14 cm adrenal mass [4, 29, 30] proved the reliability of performing a radical adrenalectomy also for lesions over 10 cm in size. In our study, adrenal mass over 10 cm in size were successfully treated in both groups. Regardless technical feasibility, as demonstrated by multivariable analysis, it should be noted that there is a growing risk of conversion in direct proportion to the size of the lesion. On the other hand, the same analysis showed that the use of an accessory trocar could reduce the risk of conversion to open procedure.

In our study, using a radiofrequency device—in addition to speeding up surgical procedures—has made it possible to effectively even the most complex surgical patients who required a greater number of trocars. The shorter operative time reported in LARFD group—in which a greater number of trocars have been used—could be due to the better handling, higher efficiency and faster coagulation

Table 8 Factors associated to length of stay: results of the Poisson Mixture regression analysis

Independent variable	Long-stay cluster (Component 1)			Short-stay cluster (Component 2)		
	Exp (Coef.reg)	95% CI	*p*	Exp (Coef.reg)	95% CI	*p*
Surgery type (LARFD vs LACD)	0.7	0.3; 1.1	0.026	0.9	0.7; 1.1	0.230
Conversion to open procedure (Yes vs No)	1.7	1.3; 2.1	0.012	1.0	0.6; 1.4	0.908
Postoperative complications (Abdominal complications vs No)	3.1	2.6; 3.6	< 0.001	1.6	1.2; 2.0	< 0.001
Postoperative complications (Non-abdominal complications vs No)	2.6	2.2; 3.0	< 0.001	1.5	1.1; 1.9	0.029
Obesity (Yes vs No)	0.9	0.6; 1.2	0.416	1.2	1.0; 1.4	0.069
Age class (≥ 70 vs < 70 years)	1.1	0.7; 1.5	0.635	1.2	1.0; 1.4	0.102

LARFD laparoscopic adrenalectomy with radiofrequency energy-based device, *LACD* laparoscopic adrenalectomy with clip device, *Exp* (*Coef. reg*) Exponential of the regression coefficient, *95% CI* 95% confidence intervals

speed of the device, especially in vascular surgical time. These advantages have made it possible to compensate and to reduce the greater operative time required to perform more surgical complex cases.

Regarding the LoS, a statistically significant difference between the two groups was found. The median hospitalization was equal to 3 and 4 days in LARFD and LACD groups, respectively. Regression analysis showed that LoS was significantly lower (by about 30%) in LARFD compared to LACD procedure for long-stay patients. However, the same benefit in a reduced LoS by using a radiofrequency device for vessel sealing was not found in patients with short hospitalization. In our opinion, the blatant reduction in operative time favored by the use of a radiofrequency device for vessel sealing could justify a better functional recovery which becomes, however, clinically evident and relevant only in patients who reported major postoperative complications. On the other hand, as expected, both postoperative complications and conversions to open procedure were factors associated with a longer LoS.

Some limitations should be considered. In our study, it was not possible to randomize patient allocation in one of the two surgical procedure groups. Therefore, reported outcomes could have been biased. However, the two groups differed for just a few characteristics (age and obesity) before undergoing the surgery procedure, and these very characteristics were used as covariates in multiple analysis models of group comparisons in order to correct comparison outcomes in relation to these covariates. Moreover, no significant differences on patient characteristics were found when comparing the two groups during availability of both procedures. Furthermore, this study describes the experience over a long timespan (1994–2019) as characterized by the sole use of LACD procedure up to December 2003 and by the use of both procedures as of January 2004, when LARFD was being used more frequently. In order to increase sample size, all study evaluations were performed considering the whole observation period and without shrinking the scope to the period when both procedures were used. Lest the long study timespan could bias some results in the comparison between the two groups, we resolved not to limit our action to bivariate analysis only—which has descriptive purposes—but to extend the evaluation of all relevant outcomes by using multiple regression models allowing to estimate the effect of the independent factor on outcome adjusting for surgery time as possible confounder.

Study's strengths are the large sample size, which to the best of our knowledge has never been reported before, and the standardization of surgical procedures. These factors made possible the comparison between the two procedures and the evaluation factors associated to them by using multiple analysis models.

Conclusion

Laparoscopic transperitoneal adrenalectomy performed by means of radiofrequency energy-based device for the sealing of the adrenal vessels is an effective procedure reducing operative time with potentially improved postoperative outcomes.

Compliance with ethical standards

Disclosures Drs. Luca Cardinali, Edlira Skrami, Elisa Catani, Flavia Carle, Monica Ortenzi, Andrea Balla, Mario Guerrieri have no conflicts of interest or financial ties to disclose.

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