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ORIGINAL ARTICLE

Impact of novel techniques on minimally invasive adrenal surgery: trends and outcomes from a contemporary international large series in urology

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Abstract
Objective To evaluate contemporary international trends in the implementation of minimally invasive adrenalectomy and to assess contemporary outcomes of different minimally invasive techniques performed at urologic centers worldwide.
Methods A retrospective multinational multicenter study of patients who underwent minimally invasive adrenalectomy from 2008 to 2013 at 14 urology institutions worldwide was included in the analysis. Cases were categorized based on the minimally invasive adrenalectomy technique: conventional laparoscopy (CL), robot-assisted laparoscopy (RAL), laparoendoscopic single-site surgery (LESS), and mini-laparoscopy (ML). The rates of the four treatment modalities were determined according to the year of surgery, and a regression analysis was performed for trends in all surgical modalities.
Results Overall, a total of 737 adrenalectomies were performed across participating institutions and included in this analysis: 337 CL (46 % of cases), 57 ML (8 %),

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263 LESS (36 %), and 80 RA (11 %). Overall, 204 (28 %) operations were performed with a retroperitoneal approach. The overall number of adrenalectomies increased from 2008 to 2013 ($p = 0.05$). A transperitoneal approach was preferred in all but the ML group ($p < 0.001$). European centers mostly adopted CL and ML techniques, whereas those from Asia and South America reported the highest rate in LESS procedures, and RAL was adopted to larger extent in the USA. LESS had the fastest increase in utilization at 6 %/year. The rate of RAL procedures increased at slower rates (2.2 %/year), similar to ML (1.7 %/year). Limitations of this study are the retrospective design and the lack of a cost analysis.

Conclusions Several minimally invasive surgical techniques for the management of adrenal masses are successfully implemented in urology institutions worldwide. CL and LESS seem to represent the most commonly adopted techniques, whereas ML and RAL are growing at a slower rate. All the MIS techniques can be safely and effectively performed for a variety of adrenal disease.

Keywords Adrenalectomy · Laparoscopy · LESS · Minimally invasive · Robotic · Outcomes

Introduction

Since the report of the first series in the early nineties [1], conventional laparoscopy (CL) for the surgical management of adrenal lesions has been safely implemented [2], given potential advantages over open surgery [3]. In addition, over the past 10 years, different minimally invasive techniques have been explored, including mini-laparoscopy (ML) [4], robot-assisted laparoscopy (RAL) [5], and laparoendoscopic single-site surgery (LESS) [6].

Few studies have explored the trends in the use of laparoscopic adrenalectomy at national level [7–9], whereas more specific data regarding the adoption of this and other minimally invasive techniques at multinational level are lacking. Moreover, most of the trend analysis in this field has been reported in general (endocrine) surgery literature [3, 7, 10]. In this scenario, it remains to be determined to what extent the introduction of all these novel techniques has impacted the surgical management of adrenal gland and what have been the outcomes following the implementation of these techniques in urologic institutions.

The aim of this study was to evaluate the contemporary international trends and outcomes in the minimally invasive surgical management of adrenal masses among urology centers worldwide.

Patients and methods

Study design

This was a retrospective multicenter study including data from 14 urology centers worldwide: Europe (Italy, Greece, Spain, UK, and Germany), Asia (Korea, Japan, and China), South America (Brazil), and USA (Ohio and California). Consecutive cases of minimally invasive adrenalectomy (any technique) performed between 2008 and 2013 were collected. Each group performed the procedures according to its own surgical indication, protocol, and technique. Raw data without any identifier were retrospectively collected and gathered in a standardized datasheet, which was specifically built for study purpose. Institutional review board approval or waiver was obtained at each participating center.

Parameters

Demographic data included age, gender, race, body mass index (BMI), history of previous abdominal surgery, and American Society of Anesthesiologists (ASA) score. Information related to the adrenal mass was also collected, namely size, side (left or right), pathology (malignant or benign), and presentation (incidentaloma or not). Procedures were categorized according to the minimally invasive technique: CL, LESS, ML, and RAL. In addition, the approach was also recorded (transperitoneal vs. retroperitoneal). The following surgical parameters were analyzed: operative time, estimated blood loss, intraoperative and postoperative complications, conversions, transfusions, length of stay, and readmission rate.

Statistical analysis

Continuous parametric variables were reported as the mean ± standard deviation (SD), while nonparametric variables were reported as the median and interquartile range (IQR). Descriptive analysis was performed using Pearson's Chi-squared test for categorical data, Student's *t* test for continuous data, and Mann–Whitney test for nonnormally distributed continuous data. The rates of the four treatment modalities were determined according to the year of surgery, and a regression analysis was performed for trends in all surgical modalities. Analyses were conducted with SAS software, version 9.1 (SAS Institute, Inc. Cary, NC, USA).

Results

Study population

Seven hundred and thirty-seven patients underwent minimally invasive adrenalectomy at participating centers during the study period. Patients' characteristics are summarized in Table 1. Patients undergoing LESS were younger (men age 48 ± 12.4 years) compared to other groups ($p < 0.001$). A higher BMI was observed in patients in the RAL group (mean BMI 30.3 kg/m^2) which was significantly higher compared to other techniques ($p < 0.001$). In addition those undergoing RAL presented a higher ASA score ($p < 0.001$) as well as a higher incidence of previous abdominal surgery (38.7 %, $p = 0.007$). On the other hand, RAL group presented a higher proportion of incidental diagnosis of adrenal mass (55 %, $p = 0.02$) and also a smaller size (median 2.7 cm, IQR 1.6–4.5; $p = 0.003$). LESS was used mostly for benign indications compared to other techniques (89.8 % of cases, $p < 0.001$).

Surgical outcomes

The surgical outcomes are summarized in Table 2. A transperitoneal approach was preferred in all but the ML group ($p < 0.001$). Overall, 204 (28 %) operations were performed with a retroperitoneal approach: 122 (36 %) CL and 82 (31 %) LESS. The median operative time was higher for RAL (150 min, 120–180), compared to CL (120 min, 85–150), LESS (117 min, IQR 90–150), and ML who had the shorter time (90 min, 80–120) ($p < 0.001$). No significant difference was found in terms of intraoperative transfusions and complications, as well as conversions. On the other hand, postoperative complication rate was higher for RAL group (21.3 %) compared to ML (12.3 %), LESS (4.2 %), and CL (8.7 %) ($p = 0.001$). Length of hospital stay was shorter for ML (median 3, 3–3) and RAL (2, 2–4) ($p < 0.001$).

Trends in surgical techniques

The regional distribution of the different minimally invasive adrenalectomy techniques is illustrated in Fig. 1.

Table 1 Main demographics

	ML ($n = 57$)	LESS ($n = 263$)	RAL ($n = 80$)	CL ($n = 337$)	p value
Patient characteristics					
Age, mean (SD)	54.24 (11.36)	48.09 (12.38)	55.44 (13.24)	53.19 (13.77)	<0.001
Gender					0.338
Male	28 (49)	122 (47)	46 (58)	158 (47)	
Female	29 (51)	141 (53)	35 (43)	179 (53)	
Race					<0.001
Caucasian	57 (100)	45 (17.1)	70 (87.5)	186 (55.5)	
Asian	0	217 (82.5)	2 (2.5)	138 (41.2)	
African American	0	0	6 (7.5)	6 (1.8)	
BMI, kg/m^2, mean (SD)	26.09 (2.88)	24.69 (30.24)	30.28 (7.55)	25.99 (4.74)	<0.001
ASA, n (%)					<0.001
1	5 (8.8)	64 (24.3)	8 (10)	44 (13.1)	
2	35 (61.4)	143 (54.4)	21 (26.3)	208 (62.1)	
3	15 (26.3)	33 (12.5)	45 (56.3)	77 (23.0)	
4	0	2 (0.8)	6 (7.5)	6 (1.8)	
Prior abdominal surgery, n (%)	12 (21)	57 (21.7)	31 (38.7)	99 (29.3)	0.007
Adrenal mass characteristics					
Incidentaloma, n (%)	25 (43.9)	95 (36.1)	44 (55)	141(42.1)	0.02
Size, cm, median (IQR)	3 (2.5–3.6)	3 (2–4.15)	2.7 (1.6–4.5)	3.5 (2.6–5)	0.003
Pathology					<0.001
Malignant	10 (17.5)	9 (3.4)	18 (22.5)	88 (26.3)	
Benign	45 (78.9)	236 (89.8)	58 (72.5)	217 (64.8)	
Side					0.067
Right	29 (50.9)	95 (36.1)	33 (41.3)	158 (47.5)	
Left	26 (45.6)	149 (56.7)	42 (52.5)	142 (42.4)	
Bilateral	0	1 (0.4)	1 (1.3)	5 (1.5)	

Table 2 Surgical outcomes

	ML ($n = 57$)	LESS ($n = 263$)	RAL ($n = 80$)	CL ($n = 337$)	*p value*
Transperitoneal approach, *n* (%)	8 (14.0)	169 (64.3)	75 (93.7)	220 (65.3)	< 0.001
OR time, Median (IQR)	90 (80–120)	117 (90–150)	150 (120–180)	120 (85–150)	<0.001
EBL, median (IQR)	50 (50–100)	50 (0–100)	50 (50–150)	50 (40–90)	0.002
Transfusion intraop, *N* (%)	1 (1.8)	2 (0.8)	4 (5)	8 (2.4)	0.117
Intraop complications, *N* (%)	6 (10.5)	14 (5.3)	5 (6.3)	11 (3.3)	0.104
Conversion, *N* (%)	0	6 (2.3)	2 (2.5)	10 (3)	0.627
Transfusion post op, *N* (%)	4 (7)	0	4 (5)	11 (3.3)	<0.001
Post op complication, *N* (%)					
Overall	9 (15.8)	11 (4.2)	17 (21.3)	29 (8.7)	0.001
Minor (Clavien 1–2)	9 (15.8)	9 (3.4)	15 (18.8)	26 (7.8)	<0.001
Major (Clavien 3–4)	0	2 (0.8)	2 (2.5)	3 (0.9)	0.565
LOS, median (IQR)	3 (3–3)	5 (4–7)	2 (2–4)	6 (4–8)	< 0.001

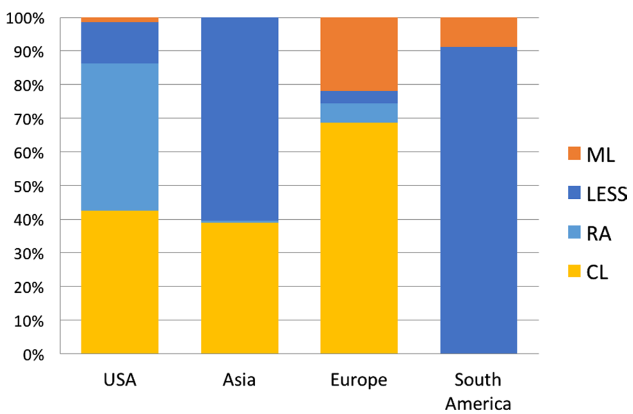


Fig. 1 Number of adrenalectomy cases during study period by regional contribution and technique (*CL* conventional laparoscopy, *RA* robot-assisted laparoscopy, *LESS* laparoendoscopic single-site surgery, *ML* mini-laparoscopy)

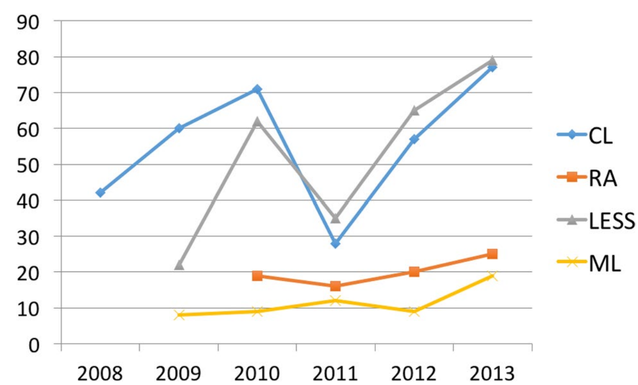


Fig. 2 Trends in the number of adrenalectomies by MIS technique during study period (*CL* conventional laparoscopy, *RA* robot-assisted laparoscopy, *LESS* laparoendoscopic single-site surgery, *ML* mini-laparoscopy)

European centers mostly adopted CL and ML techniques, whereas centers from Asia and South America reported the highest rate LESS procedures, whereas RAL was adopted to larger extent in the USA.

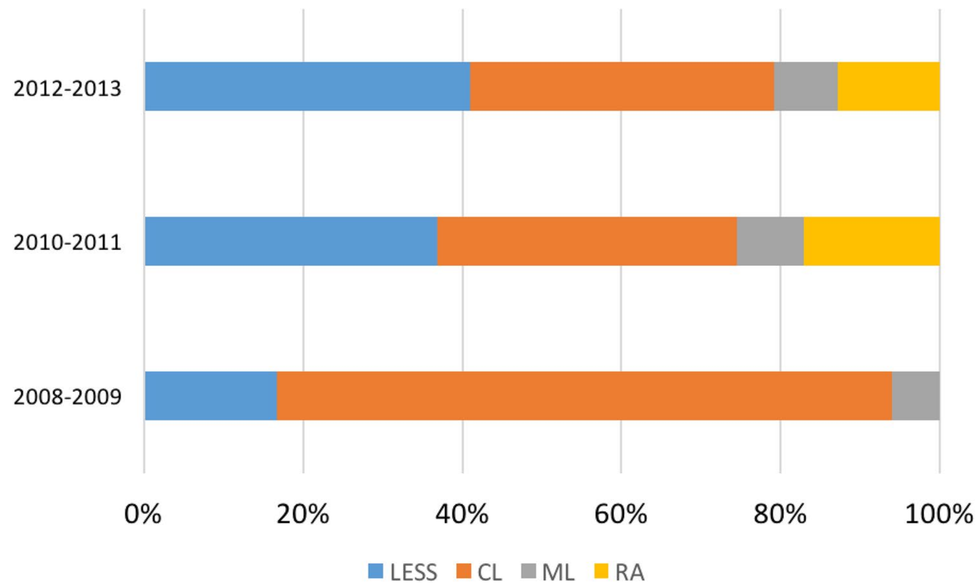
The overall numbers of adrenalectomies significantly increased from 2008 to 2013 ($p = 0.05$). Numbers of procedures according to the adopted technique are shown in Fig. 2. The overall utilization of CL and LESS has been steadily increasing and the fastest growing, as shown in Fig. 3. However, the proportion of CL adrenalectomies along the study period decreased from 100 to 39 %. Other MIS techniques showed an increase in utilization: LESS, RAL, and ML had increased to 42, 13, and 10 %, respectively. From 2008 to 2013, LESS had the fastest increase in utilization at 6 %/year. The rate of RAL procedures started to increase from 2009, but at slower rates (2.2 %/year), similar to ML (1.7 %/year).

Discussion

The present large series allows evaluating contemporary trends and outcomes in minimally invasive management of adrenal masses at urology centers in different continents. To our knowledge, no other multiinstitutional multinational series including not only CL but also other MIS techniques has been reported to date. As such, this represents a unique "real-life" dataset allowing several arguments.

Overall, present study findings suggest an overall increase in the utilization of MIS techniques for adrenal surgery, which is in line with available population-based data analyses. Monn et al. recently analyzed the national trends for adrenalectomy in the USA during the time period 2002–2011 using the Nationwide Inpatient Sample [2]. A MIS approach was used in 20 % of the 58,948 adrenalectomies included in the analysis. There was a 4 % increase

Fig. 3 Trends in the rate of each MIS technique during the study period (*CL* conventional laparoscopy, *RA* robot-assisted laparoscopy, *LESS* laparoendoscopic single-site surgery, *ML* mini-laparoscopy)



in MIS throughout the study period ($p < 0.001$). However, adrenalectomy by urologists showed a 15 % annual decrease ($p < 0.001$). Using the same database (years 1999–2005), Park et al. [10] assessed the effect of surgeon volume and specialty on the outcomes of adrenalectomy procedure. After adjusting for patient's and provider's characteristics, surgeon volume, not specialty, was an independent predictor of complications (OR 1.5, $p < 0.002$). More recently, Simhan et al. [11] analyzed 1996–2009 hospital discharge data from New York, New Jersey, and Pennsylvania of 8381 adrenalectomy cases. For each successive year, the odds of having surgery performed at a very low volume hospital decreased by 13 %. When controlling for year treated, patients were less likely to die in the hospital if treated at a very high-volume hospital (OR 0.38, 95 % CI 0.19–0.75). One of the very few multiinstitutional laparoscopic adrenalectomy series from urological centers has been reported. Greco et al. [9] analyzed 363 cases performed at 23 German hospitals. They concluded that LA performed by urologists experienced in laparoscopy can be safe for the removal of benign and malignant adrenal masses.

Over the past decade, besides the adoption of CL, other MIS options have been explored by urologic surgeons worldwide. Utilization of RAL has exponentially grown in urology following the driven by its large-scale use for radical prostatectomy [12]. Consequently, other urology indications for robotic surgery have also grown significantly [13]. Not surprisingly, we found robotic adrenal surgery to have increased to a larger extent in the USA, where diffusion of robotic platforms has been more significant compared to other regions of the globe. RAL technique has been certainly standardized [5], and the procedure can be performed safely and effectively with potential advantages of a shorter hospital stay, less blood loss, and lower occurrence of postoperative complications [14]. In our study, a higher BMI was observed in patients undergoing RAL group (mean BMI 30.3 kg/m^2) which was significantly higher compared to other techniques ($p < 0.001$). This might be simply explained by the fact that RAL was mainly performed in US Centers. Recently published Society of Gastrointestinal and Endoscopic Surgeons (SAGES) guidelines support the use of robot-assisted laparoscopy in patients with high BMI, as well those with larger tumors [15]. In our study, however, RAL group presented a higher proportion of incidental diagnosis of adrenal mass (55 %) and also a smaller median size (2.7 cm). The upper size for a laparoscopic adrenalectomy for an experienced minimally invasive surgeon is usually considered to be as high as 10–14 cm, and >6–7 cm has been considered as the upper limit in earlier stages of experience [16]. Therefore, it can be speculated that careful selection criteria were adopted, not only for RAL but also for other MIS techniques in our study.

LESS adrenal surgery has been embraced by several groups for a number of different indications and by using a variety of approaches [17]. A recent meta-analysis suggests that LESS adrenalectomy seems to be a safe and feasible alternative to its conventional laparoscopic counterpart with decreased postoperative pain, but a longer operative time [18]. This is likely to be related to the technical challenges of the procedure, which likely represent a barrier to its implementation [19]. From 2008 to 2013, LESS had the fastest increase in utilization at 6 %/year among the techniques in our study. Not surprisingly, LESS was more used for benign indications compared to other techniques (89.8 % of cases, $p < 0.001$), suggesting that surgeons approached this novel technique with some caution. To note, centers from Asia and South America reported the highest rate of LESS procedures, which is not unexpected, given the several reports coming from those regions of the world over the past few years [18]. Whether adoption of LESS in the respective countries is driven by patient demand and focus on cosmetic outcome is speculative remains to be determined. To this regard, it must be pointed out that safety and efficacy remain the key factors in the decision-making process of patients undergoing minimally invasive surgery [19]. The left side was preferred for LESS cases, and this could be explained by the fact this side might be easier with this approach, as recently suggested by Hora et al. [20].

Recently, ML has been rediscovered in an attempt to reduce the trauma on abdominal wall derived from standard laparoscopic access, improving cosmetic outcome and recovery. ML can be regarded as a viable option when looking for a virtually "scarless" surgery. Its rediscovery has been fueled by the availability of more reliable instrumentation and by the fact that ML allows minimal abdominal scar in the meanwhile preserving the key principle of triangulation [21]. A recent large multiinstitutional European series showed that a broad range of common procedures can be safely and effectively performed with contemporary ML techniques [22]. Interestingly, ML group was the only one in our study where most of the cases (86 %) were performed by using a retroperitoneoscopic approach. It remains to be determined whether this can partially account for the shorter operative time (median 90 min) and length of hospital stay (median 3 days) observed in the ML group compared to others. A recent meta-analysis suggested that a retroperitoneal approach is associated with shorter operative time (WMD: −13.10 min), less intraoperative blood loss (WMD: −40.6 ml), and shorter duration of hospital stay (WMD: −1.25 days) [23]. Certainly, the best approach for adrenalectomy procedure remains a debated issue [24].

Main limitations of this study need to be acknowledged: first, its retrospective design, which might account for inaccuracies in data reporting, and which necessarily limited the analysis to the parameters that were of sufficient quality, and second, the centers who agreed to participate are high-volume teaching institutions. Therefore, study findings should be applicable with caution in other hospital settings. Also, a cost analysis was outside the scope of this study, and this issue certainly needs further investigation. As the present study includes different health systems, it would be prohibitive to have a cost comparison, as significant parameters, for example, length of stay, are largely influenced by nonclinical factors (reimbursement systems). Despite the lack of specific cost analysis studies for adrenalectomy, potential increased costs associated with robotic surgery represent an issue that is currently being debated [25]. All these limitations being said, this study represents, to our knowledge, the largest contemporary urologic series of minimally invasive adrenalectomy procedures. Ideally, prospective comparative studies are awaited as they would represent the best way to compare these different techniques, and to ultimately determine their role in current adrenal surgery armamentarium.

In conclusion, several MIS techniques for the management of adrenal masses are successfully implemented in urology institutions worldwide. Therefore, MIS can safely and effectively replace open adrenalectomy for variety of indications wherever expertise in these techniques is available. CL still represents the most widely used MIS technique worldwide. Among the others, LESS has been the one most commonly adopted, whereas ML and RAL have been growing at a slower rate. Further investigation is necessary to understand the driving forces behind these trends. Well-designed prospective comparative studies are ideally needed to better define the role of each of these surgical options in the armamentarium of urologic surgeons managing adrenal diseases.

Authors' contributions Autorino, Darweesh, and Porpiglia are responsible for protocol/project development. Chueh, Hyun, Miyajima, Kyriazis, Puglisi, Fiori, Yang, Fei, Altieri, Chang Jeong, Branco, Chen, Ferro, Berardinelli, Liao, and Brandao collected the data. Lee, Pavan, and Autorino analyzed and managed the data. Pavan Autorino, Lee, and Darweesh drafted the manuscript Porpiglia, Sun, Greco, Cindolo, Fornara, Schips, De Cobelli, Chen, Haber, He, Oya, Liatsikos, Challacombe, and Kaouk was involved in critical revision.

Compliance with ethical standards

Ethical standards All patients included in this study signed an informed consent. The authors do not have any conflict of interest to disclose. Dr. Nicola Pavan is a SIU (Italian Society of Urology)-AUA (American Urological Association) research fellow for 2014–2015.

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