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# Perioperative outcomes of robotic and laparoscopic adrenalectomy: a large international multicenter experience

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## Abstract

**Background** The aim of the study was to describe the surgical outcomes of a retrospective series of consecutive patients treated with laparoscopic and robotic approach for adrenal masses in two tertiary referral centers.

**Methods** We retrospectively gathered data of 477 patients submitted to adrenalectomy performed at two Institutions from March 2008 to February 2018 by six highly experienced surgeons. We excluded from the analysis 43 patients that had an open approach for tumors or for anesthetic contraindications to minimally invasive surgery (MIS). Patients were selected for surgery after a radiologic and an endocrinology work up. Preoperative, perioperative and postoperative data were recorded.

**Results** Overall, 477 patients were included in the study. The robotic and the laparoscopic group included 110 and 367 patients, respectively. The preoperative characteristics were similar in both groups except for ASA score with a median (IQR) of 3 and 2 in the robotic and in the laparoscopic group, respectively ($p=0.03$). Tumor size of adrenal tumors treated robotically (4, IQR 2.6–6 cm) was significantly larger than those treated laparoscopically (3, IQR 2.3–4.1 cm) ($p=0.01$). The intraoperative complication rates were similar between robotic and laparoscopic groups (6.3% and 6%, respectively). The postoperative complication rate was 5.4% for robotic group and similarly 3.5% for laparoscopic adrenalectomy strategy. We analyzed the tumor ≥ 6 cm, with 29 patients in the robotic group and 43 in the laparoscopic one, with an overall complication rate of 19.5%. At multivariable analyses tumor size (OR 1.287; CI 1.128–1.468; $p<0.001$) was the only independent predictor of overall complication.

**Conclusion** Adrenal tumors can be safely treated either by robotic or laparoscopic strategy. MIS seems to be feasible also in larger adrenal masses (≥ 6 cm). Tumor size represents the only predictive factors for overall complication.

**Keywords** Adrenalectomy · Surgery · Minimally invasive surgery · Complication · Adrenal tumor · Adrenal gland

Adrenalectomy for benign or malignant tumors is a complex surgical procedure, especially in case of large masses, due to the proximity to major vessels and abdominal vital organs [1–3]. Since the first case of laparoscopic adrenalectomy (LA) was described by Gagner et al. in 1992 [4], LA has gradually gained popularity among endocrinological surgeons and urologist and it is now the gold standard for the treatment of most adrenal tumors [1, 2, 5]. LA has been proven to be a safe procedure with a reported low rate of complications [2]; however, LA may represent an extremely challenging surgery such as in case of large adrenal masses, in case of need for lymph node dissection or obese patients [6]. More recently the robotic platform has been introduced with the aim to overcome the intrinsic limitations of laparoscopy such as two-dimensional imaging, surgeon discomfort,

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steep learning curve and limited range of motion of surgical instruments, with the first case of robotic adrenalectomy (RA) published in 1999 [7]. In recent years, a robotic approach has increasingly been adopted for adrenal surgery, although evidence is still sparse and large comparative studies with LA in terms of perioperative safety and short outcomes are lacking [8, 9]. In this scenario, another debated topic is represented by the indication to minimally invasive adrenalectomy for large and malignant masses for whom open approach is still the standard of care [2, 6, 10]. Indeed, in this setting of patients there is still a lack of evidence of the benefit of minimally invasive surgery (MIS) [6, 9, 11, 12].

The primary aim of the present study was to report and compare perioperative outcomes of patients treated with LA or RA. The secondary aim was to explore the role of MIS for tumors ≥ 6 cm.

## Materials and methods

### Study population

After the obtainment of the institutional review board approval, between February 2008 and February 2018, all preoperative and perioperative data of patients treated with adrenalectomy were retrospectively collected at two Urology Units (Department of Oncologic, Minimally-Invasive Urology and Andrology, Careggi Hospital, Florence, Italy and Department of Urology, Drum Tower Hospital, Nanjing, China) and one General Surgery Unit (Emergency Surgery Unit, Careggi Hospital, Florence, Italy) from two high-volume centers. Written informed consent was obtained from all patients.

All cases were performed by six expert laparoscopic and robotic surgeons and all of them regularly perform both techniques.

During that period, patients undergoing adrenalectomy with open approach or for anesthesiologic contraindications to laparoscopic or robotic procedures were excluded from the analyses of the present study ($n = 43$). All the tumors removed by open adrenalectomies were larger than 10 cm.

Patients were selected for surgery after an endocrinological work up and a computed tomography (CT) or magnetic resonance imaging (MRI) was always performed preoperatively for staging purposes.

Preoperative clinical characteristics reported included gender, age, body mass index (BMI), previous abdominal surgery, side and size of the tumor. Age-adjusted Charlson Comorbidity Index (ACCI) and the American Society of Anesthesiologists (ASA) were also assessed preoperatively and recorded [13]. Overall operative time, estimated blood loss, intra- and postoperative transfusion rate, conversion to the open approach, intra- and postoperative complications, length of stay and readmission rate were recorded. The severity of complications was graded according to the modified Clavien classification system [14]. Intraoperative complications were defined as all the events occurring between induction of the anesthesia and patient awakening that could potentially cause injury and require unplanned surgical maneuvers. Postoperative complications were defined as any event occurring until the 90th postoperative day, altering the normal postoperative course and/or delaying discharge. All the preoperative, perioperative and postoperative data were recorded by medical doctors.

### Operative procedure

Regarding the surgical technique on MIS three different approaches were previously described and were chosen according to surgeon's preference: transperitoneal laparoscopic (TL), retroperitoneal laparoscopic (RL) or transperitoneal robot-assisted (RA) [2, 15, 16].

In case of RA for adrenal masses over 6 cm, the fourth robotic arm with Prograsp forceps was routinely used to facilitate surgical field exposure.

### Statistical analysis

Categorical, continuous parametric and not-parametric variables were reported as frequencies and proportions, mean and standard deviation (SD) or as median and interquartile range (IQR), respectively. Unpaired *T* test, Mann–Whitney and Pearson's $\chi^2$ tests were used to compare variables, as appropriate. Statistical significance in this study was set as $p \leq 0.05$. All reported *p* values are two-sided. Analyses were performed with SPSS version 25.0 (SPSS Inc., Chicago, IL, USA).

## Results

### Preoperative tumors and patients features

Overall, 477 patients submitted to RA or LA during the study period were included in the analysis and their features are summarized in Table 1 and Supplementary Materials (Figs. 1–3): the robotic group included 110 patients, while the laparoscopic group included 367 patients. The preoperative characteristics were similar in both groups expect for the ASA score with a median (IQR) of 3 and 2 in the robotic and in the laparoscopic group, respectively ($p = 0.03$). Indeed, median (IQR) clinical tumor size was greater in the robotic group (4.0, IQR 2.6–6 cm) compared to the laparoscopic one (3.0, IQR 2.3–4.1 cm) ($p = 0.01$).

**Table 1** Patients treated with minimally invasive adrenalectomy

| | Robotic group ($n=110$) | Laparoscopic group ($n=367$) | $p$ value |
|---|---|---|---|
| Preoperative data | | | |
| Gender, *n* % | | | 0.25 |
| M | 58 (52.7%) | 171 (46.6%) | |
| F | 52 (47.3%) | 196 (53.4%) | |
| Previous abdominal surgery | | | 0.67 |
| No | 77 (70%) | 249 (67.8%) | |
| Yes | 33 (30%) | 118 (32.2%) | |
| Side | | | 0.03 |
| Right | 54 (49.1%) | 177 (48.2%) | |
| Left | 54 (49.1%) | 190 (51.8%) | |
| Bilateral | 2 (1.8%) | – | |
| Age (years), median; IQR | 51 (40–61) | 53 (44–62) | 0.18 |
| Hb preoperatory, median; IQR | 13.9 (12.6–14.9) | 13.5 (12.3–14.5) | 0.50 |
| ASA, median; IQR | 3 (2–3) | 2 (2–3) | **0.03** |
| CCI adjusted, median; IQR | 2 (1–3) | 2 (2–3) | 0.07 |
| BMI (kg/m$^2$), median; IQR | 24.5 (22.1–27.7) | 24.3 (22.1–26.7) | 0.08 |
| Tumor size (cm); median, IQR | 4 (2.6–6) | 3 (2.3–4.1) | **0.01** |
| Intra and postoperative data | | | |
| Retroperitoneal approach; *n* % | – | 117 (31.8%) | – |
| Operative time (minute), median; IQR | 110 (90–130) | 110 (85–130) | 0.94 |
| Hb postoperative, *n* % | 12.3 (11.1–13.3) | 12.5 (11.3–13.5) | 0.27 |
| LOS, median; IQR | 4; (3–4) | 4; (3–5) | 0.52 |
| Histology | | | 0.63 |
| Benign | 96 (88.9%) | 320 (87.2%) | |
| Malignance | 12 (11.1%) | 47 (12.8%) | |
| Readmission, *n* % | 2 (1.8%) | 5 (1.4%) | 0.71 |

Significant $p$ values are highlighted in bold

Overall, in 117 (31.8%) patients a retroperitoneal approach was adopted in the laparoscopic group, while all robotics cases were done using a transperitoneal approach.

## Intraoperative and postoperative complications

In Table 2, we recorded the complication of both approaches.

The overall complication rate was similar in the robotic group (11.8%) compared to the laparoscopic group (9.5%). We recorded 7 (6.3%) intraoperative complications in the robotic group: 4 (3.6%) intraoperative transfusion for bleeding requiring blood transfusion (Clavien 2) and 3 (3.3%) cases of intraoperative hypertension after the removal of the adrenal masses that needed an additional medical drug treatment (Clavien 2). In the laparoscopic group, 22 (6.0%) intraoperative complications were recorded; in particular, intraoperative transfusion for major bleeding was required in 14 (3.8%) cases, 5 (1.4%) cases of hypertension after the removal of the masses were recorded, while 2 (0.5%) accidental cava vein damage managed with an intracorporal suture and 1 (0.3%) spleen injury requiring position of hemostatic agents (Floseal and Tachosil) were also registered. Only 3 cases (0.8%) of conversions to open approach were registered in the laparoscopic group, while no need to conversion was observed with RA. Blood loss was significantly higher in the laparoscopic group compared to the robotic one (50 ml and 80 ml; $p<0.001$), although not clinically relevant.

No differences in terms of postoperative complication rate were found between the laparoscopic [13 (3.5%)] and the robotic groups [6 (5.4%)] ($p=0.74$). In detail, in the laparoscopic group, 5 (1.4%) patients underwent blood transfusion (Clavien 2) for postoperative anemia, 2 (0.6%) patient developed deep vein thrombosis with embolism treated with heparin (Clavien 2), 3 (0.8%) patients reported wound infection requiring bed side medication during the recovery and in the outpatient clinic (Clavien 2) and 3 (0.8%) patients experimented a postoperative fever successfully treated with broad spectrum antibiotics (Clavien 2). In the robotic group, 2 (1.8%) patients required postoperative blood transfusion, 3 (2.7%) patients had fever treated with antibiotic therapy and 1 (0.9%) patient

**Table 2** Complication with minimally invasive adrenalectomy

| | Robotic group ($n=110$) | Laparoscopic group ($n=367$) | $p$ value |
|---|---|---|---|
| Intra and postoperative complication | | | |
| Conversion, *n %* | – | 3 (0.8%) | 0.34 |
| Blood loss (Ml), median; IQR | 50 (30–110) | 80 (60–100) | **< 0.001** |
| Intraop. complications, *n %* | 7 (6.3%) | 22 (6.0%) | 0.89 |
| *Intraop. transfusion, n %* | 4 (3.6%) | 14 (3.8%) | 0.93 |
| *Intraop. hypertension after removal of adrenal tumor, n %* | 3 (2.7%) | 5 (1.4%) | 0.32 |
| *Cava vein damage with intracorporeal suture, n %* | – | 2 (0.5%) | 0.43 |
| *Spleen injury requiring hemostatic agents, n %* | – | 1 (0.3%) | 0.58 |
| Postop. complications, *n %* | 6 (5.4%) | 13 (3.5%) | 0.74 |
| *Postop. transfusion, n %* | 2 (1.8%) | 5 (1.4%) | 0.72 |
| *Deep vein thrombosis treated with heparin, n %* | 1 (0.9%) | 2 (0.6%) | 0.57 |
| *Wound infection requiring bed side medication, n %* | – | 3 (0.8%) | 0.34 |
| *Postop. fever management with broad spectrum antibiotics, n %* | 3 (2.7%) | 3 (0.8) | 0.11 |

Significant $p$ values are highlighted in bold

**Table 3** Multivariable analysis for overall complications

| Variable | OR (95% CI) | $p$ |
|---|---|---|
| ASA score | 1.098 (0.617–1.956) | 0.750 |
| Previous abdominal surgery | 0.697 (0.684–3.916) | 0.268 |
| Age | 0.990 (0.953–1.028) | 0.593 |
| CCI adjusted | 1.349 (0.845–2.155) | 0.210 |
| BMI | 0.228 (0.850–1.040) | 0.228 |
| Size | 1.287 (1.128–1.468) | 0.001 |
| Surgical approach | | 0.967 |
| Laparoscopic | Reference | |
| Robotic | 0.911 (0.325–2.555) | 0.859 |
| Surgical technique | | 0.896 |
| Transperitoneal | Reference | |
| Retroperitoneal | 0.951 (0.443–2.040) | |

developed deep vein thrombosis requiring heparin treatment. No Surgical Clavien 4 or 5 was collected in the whole series.

At multivariable analyses (Table 3) tumor size (OR 1.287; CI 1.128–1.468; $p < 0.001$) was the only independent predictor of postoperative complication.

### Outcomes of adrenal tumors ≥ 6 cm

In Table 4, we analyzed and we described the outcomes of adrenalectomy for tumors ≥ 6 cm, 29 patients in the robotic group and 43 in the laparoscopic group. The overall complication rate was 19.5%; no different were found between the two groups divided for the approach (except for BMI).

## Discussion

LA represents the gold standard for the treatment of most adrenal masses; however, in cases of large or malignant lesions, LA can be an extremely challenging surgery. In this context, robotic platform has been developed with the aim to overcome main technical limitations of laparoscopy. Since the first case of RA in 1999, with the progressive spread of robotic platform, RA has gradually been adopted as an alternative to LA and several studies reported its feasibility and perioperative safety [17]. However, large comparative series between LA and RA are lacking in current literature and evidences providing a real benefit of RA over LA have not been provided so far [16, 18]. To the best of our knowledge, the present study represents the largest series reporting the outcomes of minimally invasive adrenalectomy for the management of adrenal masses from two high-volume centers.

In our series, no significant differences were found in terms of intraoperative features between the two groups of patients, except for EBL that was slightly higher in the laparoscopic group (80 versus 50 cc), although not clinically meaningful since there were no differences in terms of perioperative transfusion rate. These results are superimposable to those reported in other monocentric series [8, 19]. Moreover, in our series, median operative time was 110 min in both groups; this result is in line with those reported in a meta-analysis [16] but it disagrees with a more recent systematic review by Economopoulos et al., involving 1162 patients submitted to RA ($n=747$) or LA ($n=415$), who reported significantly longer operative times in the robotic group [20]. In our opinion, these results should be attributable to the high expertise of robotic surgeons involved in our series.

**Table 4** Patients treated with minimally invasive adrenalectomy for tumor ≥ 6 cm

| | All patients with tumor ≥ 6 cm ($n=72$) | Robotic group, ≥ 6 cm ($n=29$) | Laparoscopic group, ≥ 6 cm ($n=43$) | $p$ value |
|---|---|---|---|---|
| Preoperative data | | | | |
| Gender, *n %* | | | | 0.28 |
| M | 40 (55.6%) | 15 (51.7%) | 25 (58.1%) | |
| F | 32 (44.4%) | 14 (48.3%) | 18 (41.9%) | |
| Previous abdominal surgery | | | | 0.97 |
| No | 47 (65.3%) | 19 (65.5%) | 28 (65.1%) | |
| Yes | 25 (34.7%) | 10 (34.5%) | 15 (34.9%) | |
| Side | | | | 0.46 |
| Right | 34 (47.2%) | 13 (44.8%) | 21 (48.8%) | |
| Left | 37 (51.4%) | 15 (51.7%) | 22 (51.2%) | |
| Bilateral | 1 (1.4%) | 1 (3.4%) | – | |
| Age (years), median; IQR | 52 (42–63) | 53; (42–61) | 50 (42–68) | 0.35 |
| Hb preoperatory, median; IQR | 13.1 (12.1–14.5) | 13 (12.4–14.9) | 13.2 (12–14.5) | 0.23 |
| ASA, median; IQR | 2 (2–3) | 3 (2–3) | 2 (2–3) | 0.15 |
| CCI adjusted, median; IQR | 2 (1–3) | 2 (1–3) | 3 (1–3) | 0.42 |
| BMI ($kg/m^2$), median; IQR | 24.1 (21.9–27.2) | 26.7 (23.1–27.7) | 23.8 (21.8–25.7) | **0.03** |
| Tumor size (cm); median, IQR | 7.9 (6.1–9) | 7.5 (6.5–9) | 8 (6–9.5) | 0.32 |
| Intra and postoperative data | | | | |
| Retroperitoneal approach; *n %* | – | – | – | – |
| Operative time (min), median; IQR | 120 (100–145) | 120 (100–140) | 120 (100–150) | 0.23 |
| Blood loss (Ml), median; IQR | 85 (50–120) | 50 (30–110) | 90 (80–130) | 0.07 |
| Conversion, *n %* | 2 (2.8%) | – | 2 (4.7%) | 0.23 |
| Intraop. complications, *n %* | 12 (16.7%) | 4 (13.8%) | 8 (18.6%) | 0.59 |
| *Intraop. transfusion, n %* | 8 (11.1%) | 3 (10.3%) | 5 (11.6%) | 0.86 |
| *Intraop. hypertension after removal of adrenal tumor, n %* | 3 (4.2%) | 1 (3.4%) | 2 (4.7%) | 0.80 |
| *Cava vein damage with intracorporeal suture, n %* | 1 (1.4%) | – | 1 (2.3%) | 0.40 |
| Postop. complications, *n %* | 2 (2.8%) | 1 (3.4%) | 1 (2.3%) | 0.77 |
| *Postop. Transfusion, n. %* | 2 (2.8%) | 1 (3.4%) | 1 (2.3%) | 0.77 |
| Hb postoperative, median; IQR | 11.9 (10.9–13) | 11.7 (10.8–12.4) | 12 (11–13.1) | 0.07 |
| LOS, median; IQR | 5 (3–5) | 4; (3–5) | 4; (4–6) | 0.27 |
| Histology | | | | 0.15 |
| Benign | 56 (77.8%) | 25 (86.2%) | 31 (72.1%) | |
| Malignance | 16 (22.2%) | 4 (13.8%) | 12 (27.9%) | |
| Readmission, *n %* | 7 (9.7%) | 2 (1.8%) | 5 (1.4%) | 0.21 |

Significant $p$ values are highlighted in bold

Furthermore, we reported similar perioperative outcomes of LA or RA in terms of complication rate, hospital stay, conversion rate to open approach and hospital readmission; in detail, only 3 cases (0.8%) of conversions to open approach were registered in the LA group, while no need to conversion was observed in the RA group. Moreover, we observed a low rate of postoperative complications, mostly minor, in both groups (5.4% and 3.5% in the robotic and laparoscopic group). These data, taken together, underline the excellent perioperative outcomes of adrenalectomy when performed with a minimally invasive approach at high-volume centers. Then we sought to analyze the results of LA or RA when performed for large (≥ 6 cm) adrenal masses.

In our experience, overall complication rate was 17.2% and 20.9% in the robotic and laparoscopic groups, respectively ($p=0.69$). Moreover, only two cases (4.7%) in the laparoscopic group needed a conversion to open approach, while conversion from robotic to open approach was never registered in our series. These results are similar to those reported by Agcaoglu et al. in a comparative series of robotic and laparoscopic adrenalectomy for the treatment of > 5 cm adrenal tumors (9); the authors also reported a lower conversion rate in the robotic group compared to the laparoscopic

one. We believe that a larger sample size would have produced similar results also in our experience. Notably, tumor size was the only independent predictor of surgical complications at multivariable analyses, thus stressing to correct prepare and use the best available solutions for large tumor as the fourth operative robotic arm, an experienced team and a good preoperative planning.

The present study is not devoid of limitations. First, no comparison or randomization are provided between patients undergone laparoscopic and patients treated with robotic approach; as such, it is possible that some surgeons may have preferred to approach the more difficult cases (e.g., larger masses or patients with higher BMI) with a robotic approach due to the intrinsic benefit of robotic platform. However, the study confirms the feasibility and safety of both laparoscopic and robotic surgeries for the management of adrenal masses also for the larger ones. Secondly, procedures were all performed by experienced surgeons at two tertiary referral centers; as such our results might not be applicable to all surgeon- or center-related scenarios. Finally, the retrospective nature of the study may have limited the significance of the outcomes examined. Each of these factors might have weakened the overall reliability of reported findings.

Acknowledging these limitations, the present study represents the largest series so far reporting the outcomes of minimally invasive adrenalectomy for the management of adrenal masses. MIS has shown excellent peri- and postoperative outcomes; although robotic seems to be preferred in the larger tumor, it is still difficult to provide evidence-based recommendations regarding the use of robotic assistance in this setting of patient if the surgeon presented a high expertise with laparoscopy. Moreover, it is of pivotal importance that the surgical approach is carried out by surgeons with wide experience in the treatment of adrenal masses. Larger randomized series would be needed to confirm our results.

## Conclusion

In conclusion, adrenal tumors can be safely treated either by robotic or laparoscopic strategy by expert surgeons and MIS seems to be feasible also in larger adrenal masses ($\geq 6$ cm). Tumor size represents the only predictive factors for overall complication.

### Compliance with ethical standards

**Disclosures** Simone Sforza, Andrea Minervini, Riccardo Tellini, Changwei Ji, Carlo Bergamini, Alessio Giordano, Qun Lu, Wei Chen, Feifei Zhang, Hao Ji, Fabrizio Di Maida, Paolo Prosperi, Lorenzo Masieri, Marco Carini, Andrea Valeri and Hongqian Guo have no conflicts of interest or financial ties to disclose.

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