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Surgery in Motion

# Robot-assisted Partial Adrenalectomy for the Treatment of Conn's Syndrome: Surgical Technique, and Perioperative and Functional Outcomes

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**Abstract**

***Background:*** In the era of minimally invasive surgery, partial adrenalectomy has certainly been underused. We aimed to report surgical technique and perioperative, pathologic, and early functional outcomes of a two-center robot-assisted partial adrenalectomy (RAPA) series.
***Objective:*** To detail surgical technique of RAPA for unilateral aldosterone-producing adenoma (UAPA), and to report perioperative and 1-yr functional outcomes.
***Design, setting, and participants:*** Data of 10 consecutive patients who underwent RAPA for UAPA at two centers from June 2014 to April 2017 were prospectively collected and reported.
***Surgical procedure:*** RAPA was performed using a standardized technique with the da Vinci Si in a three-arm configuration.
***Measurements:*** Baseline and perioperative data were reported. One-year functional outcomes were assessed according to primary aldosteronism surgery outcome guidelines. A descriptive statistical analysis was performed.
***Results and limitations:*** All cases were completed robotically. Median nodule size was 18 mm (interquartile range [IQR] 16–20). Intraoperative blood loss was negligible. A single (10%) postoperative Clavien grade 2 complication occurred. Median hospital stay was 3 d (IQR 2–3). Patients became normotensive immediately after surgery (median pre- and postoperative blood pressure: 150/90 and 120/70 mmHg, respectively). At both 3-mo and 1-yr functional evaluation, all patients achieved biochemical success (aldosterone level, plasmatic renin activity, and aldosterone-renin ratio within normal range). Complete clinical success was achieved in nine patients, but one required low-dose amlodipine at 6-mo evaluation. At a median follow-up of 30.5 mo (IQR 19–42), neither symptoms nor imaging recurrence was observed.
***Conclusions:*** We demonstrated feasibility and safety of RAPA for UAPA; this technique had very low risk of complications and excellent functional results. Increased availability of robotic platform and increasing robotic skills among urologists make RAPA a treatment option with potential for widespread use in urologic community.
***Patient summary:*** Robot-assisted partial adrenalectomy is a safe, feasible, and minimally invasive surgical approach. Promising perioperative and functional outcomes suggest an increasing adoption of this technique in the near future.


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## 1. Introduction

The International Consultation on Urological Diseases and European Association of Urology consultation recommend total adrenalectomy (TA) as the first-line therapy for any benign adrenal mass requiring surgical resection [1].

In analogy with partial nephrectomy (PN), with the increasing adoption of robotic surgery [2,3] surgical experience with organ-sparing procedures has grown exponentially over the last decade, and this has led to the broadening of the indication of a conservative approach even in more complex cases [4]. Although clinical benefits of preserving renal function with PN appear as strong outcomes compared with preservation of adrenal function, a systematic review showed that partial adrenalectomy (PA) may obviate the need for steroid replacement and provides very-low local recurrence, suggesting that PA might be considered as a primary-option treatment when technically feasible [5].

According to several reports, the most common indication to perform PA is represented by unilateral aldosterone-producing adenoma (UAPA), also known as Conn's syndrome; usually, UAPA is a small, anterior, and solitary mass located at the gland margin. This anatomical scenario makes it particularly suitable for an enucleative approach [6–8].

The increased robotic skills in urologic community and increased experience with robotic PN make RAPA an attractive surgical option for urologists. Since several studies have shown in the past that maximal preservation of adrenal parenchyma may have a significant impact on patient quality of life, we hypothesized that a conservative approach could be a feasible and reasonable option for the treatment of UAPA [9].

The aim of the present series is to detail step by step our surgical technique of robot-assisted partial adrenalectomy (RAPA) for UAPA with the accompanying Supplementary video, and to report the perioperative, pathologic, and functional outcomes in 10 consecutive patients with a minimum 1-yr follow-up.

## 2. Patients and methods

### 2.1. Study population and inclusion criteria

Between June 2014 and April 2017, data of 10 consecutive patients were prospectively collected and maintained in separate institutional databases at two tertiary-care referral centers. All patients provided written informed consent. Institutional Review Board approval protocol number was RS1080/18. Indications for RAPA were limited to small (<3 cm) aldosterone-secreting tumors and symptomatic patients requiring hypotensive treatment. Contraindications to an adrenal-sparing approach included infiltrative or larger tumors (>3 cm) when the potential adrenal remnant was judged to be unpredictable.

### 2.2. Preoperative assessment

Performance of UAPA did not modify presurgical management of patients as for TA. Hypertension and hypokalemia were controlled with medications in all patients before surgery according to the Endocrine Society Guidelines [10]. In both centers, a multidisciplinary management plan involving an endocrinologist was followed in a patient presenting with an adrenal mass. All patients underwent abdomen computed tomography or magnetic resonance imaging to assess location and size of the mass, and a routine blood sample assessing aldosterone level and plasmatic renin activity (PRA). Adrenal venous sampling (AVS) was performed in all patients to confirm laterality of disease [11].

A weight-based single dose of cefazolin (2–3 g) was administered intravenously before treatment, and anticoagulation treatment was discontinued and replaced with low-molecular-weight heparin 7 d before surgery. Bowel preparation was not performed.

### 2.3. Surgical technique

Two separate surgical teams were involved in the cohort (M.G., S.G., G. S.—eight cases; A.C., B.D.C.—two cases); the same robotic platform (da Vinci Si Surgical System; Intuitive Surgical, Sunnyvale, CA, USA) was used. Patients, port placement, and instruments used meticulously reproduced PN setup [12]. Patients were placed in a mildly flexed extended flank position, and side docking with transperitoneal five-port access was performed using a 30° scope. Camera port was placed on the pararectal line at the level of the umbilicus, in order to improve visualization of the upper retroperitoneum, and two robotic ports were placed along the midclavicular and anterior axillary line, as shown in the Supplementary video. Two 12-mm ports for the assistant surgeon were placed at the midline, between the camera and the robotic ports. A three-arm configuration was used, and Hot Shears monopolar curved scissors, ProGrasp forceps, and a large needle driver were used to suture the remnant adrenal gland. The two 12-mm assistant ports allowed the introduction of one or two suction irrigation devices, a Weck clip (Teleflex, Wayne, PA, USA) applier, and a 10-mm LigaSure device (Medtronic, Minneapolis, MN, USA).

#### 2.3.1. Right side

A straightforward approach to the right adrenal gland usually requires limited bowel mobilization. The triangular ligament was divided and the liver retracted superiorly by the bed assistant, providing wide exposure of the inferior vena cava (IVC) and optimization of the surgical workspace. Gerota's fascia was incised at the level of the upper pole of the kidney. Major anatomical landmarks on the right side were represented by the posterior peritoneum overlying the upper pole of the adrenal gland and the lateral border of the IVC. Medial surface of the gland was bluntly dissected, and small accessory veins occasionally identified were sealed with 10-mm LigaSure.

#### 2.3.2. Left side

The splenic flexure was incised and the splenorenal ligaments were divided. The spleen, bowel, and pancreas tail were deflected medially. Gerota's fascia was incised at the level of the upper pole of the kidney, and the adrenal gland was identified.

#### 2.3.3. Tumor dissection

The adenoma was progressively mobilized starting from the medial adrenal surface following the pseudocapsule plane. In this phase, it is of paramount importance to minimize dissection within Gerota's fascia, preserving the blood supply in this area in order to maintain the vasculature of residual unaffected adrenal parenchyma. Fat layers were preserved for handling the gland, while avoiding any parenchymal injury. The mass was enucleated, attempting to keep the integrity of tumor margins with minimal damage to surrounding tissues. A meticulous combination of blunt and sharp dissection using monopolar scissors was employed in order to maximize adrenal parenchyma preservation. Simultaneous use of two section devices (one for irrigation and one for suction) contributed to maintaining a bloodless surgical field. Blood pressure was carefully monitored intraoperatively to ensure hemodynamic stability during the procedure.

Table 1 – Primary Aldosteronism Surgery Outcome International Consensus (PASO recommendation)

| Outcome measure | Definition/recommendation |
| --- | --- |
| Complete clinical success | Normal blood pressure without the aid of antihypertensive medication |
| Partial clinical success | The same blood pressure with less antihypertensive medication or a reduction in blood pressure with either the same amount of or less antihypertensive medication |
| Absent clinical success | Unchanged or increased blood pressure levels with either the same amount of or an increase in antihypertensive medication |
| Complete biochemical success | Correction of hypokalemia (if present before surgery) and normalization of the ARR. In patients with an elevated ARR, aldosterone secretion should be suppressed in a postsurgery confirmatory test |
| Partial biochemical success | Correction of hypokalemia (if present before surgery) and an elevated ARR with one or both of the following (compared with before surgery):<br>1. ≥50% decrease in baseline plasma aldosterone level<br>2. Abnormal but improved postsurgery confirmatory test result |
| Absent biochemical success | Persistent hypokalemia (if present before surgery) and/or persistent elevated ARR with failure to suppress aldosterone secretion with a postsurgery confirmatory test |
| Outcome assessment | Outcome assessment should first be performed in the 3 mo after surgery, but final outcome should be assessed at 6–12 mo |
| Annual reassessment | Outcome should be reassessed annually |

ARR = aldosterone-renin ratio; PASO = Primary Aldosteronism Surgery Outcome.

The dissection was carried out without any attempt of isolation of adrenal vessels, in order to avoid any accident or injury to adrenal vessels. After removal, the specimen was inspected to ensure absence of any macroscopic margin violation before securing it into an Endocatch bag.

#### 2.3.4. *Suture of adrenal remnant*

The remaining gland after the removal of aldosterone-producing adenoma usually consisted of a laterally cut functioning adrenal parenchyma dissected from the mass. Eventually, surgical bed was inspected for any significant bleeding, and the remnant adrenal margins were approximated with a sliding-clip running suture (3/0 Monocryl). Final hemostasis was checked by lowering the pneumoperitoneum, and a drain was left in place. The bagged specimen was extracted through the camera port.

### 2.4. *Postoperative course and follow-up schedule*

Pain control was achieved using intravenous nonopioid analgesics with a gradual transition to oral painkillers from the 1st postoperative day (POD). Oral intake was initiated on POD-1 with clear liquids and gradually advanced to a normal diet. Patients were encouraged to ambulate on the first POD. The drain and urethral catheter were generally removed on POD-1. Low-molecular-weight heparin was administered for 2 wk. Routine postoperative care included continuous monitoring of blood pressure. Aldosterone serum level and PRA were assessed 24 h after surgery. Drain was removed when output was <100 ml/24 h. If no complications occurred, the patient was usually discharged on the second or third POD.

Follow-up schedule included urologic and endocrinologic visits at 3, 6, and 12 mo; laboratory tests were performed at 3 mo and 1 yr, while blood pressure monitoring was recorded at each visit. Cardiologist advice was scheduled when needed.

### 2.5. *Data collection and outcome assessment*

Collected demographic parameters were age, body mass index, gender, and American Society of Anesthesiologists score. Main surgical outcomes, including operative time, estimated blood loss, length of hospital stay, and complication rate according to the Clavien-Dindo system, were reported [13]. Pathology findings, including pathologic tumor size, histology, and margin status, were analyzed. Primary endpoints were the surgical and pathologic outcomes of RAPA assessed by means of perioperative morbidity, complications, and positive surgical margin rate (defined as absence of any remnant of adrenal parenchyma surrounding the capsule). Secondary endpoints were represented by functional outcomes assessed at 3, 6, and 12 mo according to recently published Primary Aldosteronism Surgery Outcome (PASO) guidelines [14]. A clinical success was defined as normalization of blood pressure after surgery without the aid of any hypotensive medication. A biochemical success was defined if all the following criteria were present: (1) correction of hypokalemia (if present before surgery), and (2) normalization of the aldosterone-renin ratio (ARR). In case of patients with an elevated preoperative ARR, aldosterone secretion should be suppressed in a postsurgery confirmatory test (Table 1).

Descriptive analyses were used. Frequencies and proportions were reported for categorical variables. Median values and interquartile ranges (IQRs) were reported for continuously coded variables.

## 3. Results

### 3.1. *Baseline data*

Demographic data are reported in Table 2. Median clinical adenoma size was 18 mm (IQR 16–20 mm). Median preoperative hemoglobin, serum aldosterone, and PRA were 14 g/dl (IQR 13.6–14.3 g/dl), 321.5 pg/dl (IQR 299.8–438 pg/dl), and 0.15 g/ml (IQR 0.15–0.15 ng/ml h), respectively. Median ARR was 201 (IQR 188–292). All patients at the time of surgery were under hypotensive treatment with a median blood pressure of 150/90 mmHg (Table 2).

### 3.2. *Intra- and perioperative outcomes*

All cases were completed robotically. Median operative time was 65 min (IQR 60–65). Intraoperative blood loss was negligible, and no patient received blood unit transfusion in the postoperative setting. Postoperative course was uneventful in all patients but one, who required antibiotic treatment due to postoperative fever (Clavien grade 2). Median hospital stay was 3 d (IQR 2–3). All patients were normotensive and hypotensive treatment free at discharge.

### 3.3. *Pathologic results*

In all patients, pathologic evaluation showed the presence of a capsulated adenoma of the adrenal cortex. A thin rim

**Table 2 – Baseline and preoperative data**

| | |
|---|---|
| Patients ($n$) | 10 |
| Median age, yr (IQR) | 43 (38–49) |
| Gender, male/female | 3/7 |
| Median BMI (IQR) | 25.7 (24.22–30.85) |
| Median ASA score (IQR) | 3 (2–3) |
| Median adenoma size, mm (IQR) | 18 (16–20) |
| Median preop Hb, g/dl (IQR) | 14 (13.6–14.3) |
| Median preop aldosterone, pg/dl (IQR; n.v. 17.6–232) | 321.5 (299.8–438) |
| Median preop systolic blood pressure, mmHg (IQR) | 150 (140–160), with hypotensive treatment |
| Median preop diastolic blood pressure, mmHg (IQR) | 90 (90–95) |
| Median preop PRA, ng/ml h (IQR; n.v. 0.2–2.8) | 0.15 (0.15–0.15) |
| Median preop ARR (IQR; n.v. <23.6) | 201 (188–292) |

ARR = aldosterone-renin ratio; ASA = America Society of Anesthesiologist Society; BMI = body mass index; Hb = hemoglobin; IQR = interquartile range; n.v. = normal values; PRA = plasmatic renin activity.

**Table 3 – Pathologic, perioperative, and functional data**

| | |
|---|---|
| Patients, $n$ | 10 |
| Histology | |
| Cortical adenoma, $n$ (%) | 10 (100) |
| Positive surgical margins, $n$ (%) | 0 (0) |
| Conversion to open surgery, $n$ (%) | 0 (0) |
| Median operative time, min (IQR) | 65 (60–65) |
| Median EBL, ml (IQR) | 150 (150–200) |
| Clavien grade complications | |
| 0 | 9 |
| 2 | 1 |
| Median hospital stay, d (IQR) | 3 (2–3) |
| Median Hb at discharge, g/dl (IQR) | 12.7 (12.3–13.3) |
| 3-mo median aldosterone levels, pg/ml (IQR; n.v. 17.6–232) | 153 (125–164) |
| 3-mo median systolic postop blood pressure, mmHg (IQR) | 120 (115–125) |
| 3-mo median diastolic postop blood pressure, mmHg (IQR) | 70 (65–80) |
| 3-mo median postop PRA, ng/ml h (IQR; n.v. 0.2–2.8) | 1.53 (0.88–2.1) |
| 3-mo median postop ARR (IQR; n.v. <23.6) | 9.5 (7.8–15.3) |
| 1-yr median aldosterone levels, pg/ml (IQR; n.v. 17.6–232) | 148 (115–174) |
| 1-yr median systolic postop blood pressure, mmHg (IQR) | 120 (115–125) |
| 1-yr median diastolic postop blood pressure, mmHg (IQR) | 70 (65–80) |
| 1-yr median postop PRA, ng/ml h (IQR; n.v. 0.2–2.8) | 1.42 (0.6–2) |
| 1-yr median postop ARR (IQR; n.v. <23.6) | 9.2 (6.4–18.1) |

ARR = aldosterone-renin ratio; EBL = estimated blood loss; Hb = hemoglobin; IQR = interquartile range; n.v. = normal values; PRA = plasmatic renin activity.

(<1 mm) of healthy parenchyma surrounding the mass was visible in all patients (Fig. 1).

### 3.4. *Follow-up*

At 3-mo outcome assessment, no patients required further hypotensive treatment. Aldosterone, PRA levels, and ARR returned within the normal range after surgery (3-mo median aldosterone: 153 pg/ml [normal values: 17.6–232; IQR 125–164]; 3-mo median PRA: 1.53 ng/ml h [normal values: 0.2–2.8; IQR 0.88–2.1]; 3-mo median ARR: 9.5 [normal values: <23.6; IQR 7.8–15.3]; Table 3). At 1-yr follow-up, nine patients were normotensive and treatment free (complete biochemical and clinical success according to the PASO guidelines); a single patient had biochemical success and partial clinical success (started low-dose amlodipine at 6-mo evaluation). At a median follow-up of 30.5 mo (IQR 19–42), functional outcomes were unaltered and no imaging recurrence was observed.

## 4. Discussion

According to current guidelines, TA is still the standard of care for any adrenal mass candidate to surgical treatment [15]. A conservative approach may be considered an option in selected small adrenal masses with clinical symptoms of Conn's disease, where the risk of malignancy is negligible and the likelihood of maintaining normal adrenal cortical function is high [16]. Traditionally, indications to a conservative management respond to the need of minimizing negative

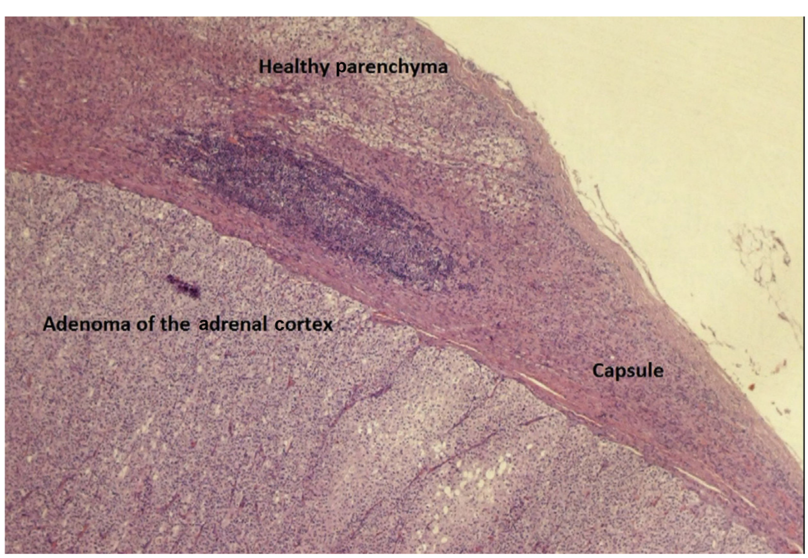


**Fig. 1 – Pathologic findings highlighting a small rim of healthy parenchyma surrounding the adrenal adenoma capsule.**

clinical consequence of radical treatments [17]. This has been the history of PN, initially considered an option in imperative settings and today established as a standard option for cT1 renal tumors "whenever technically feasible" [18,19]. Notably, technical challenges are certainly the main drivers of clinical underuse of PN in contemporary era [12], and consequently, potential wide diffusion of PA is certainly an attractive surgical option also outside of high-volume centers. While adoption of an adrenal-sparing approach for patients with bilateral or multifocal adrenal disease may be supported by the potential side effects of adrenal insufficiency (Addisonian crisis), the role of PA in patients with a small UAPA mass may be questionable. However, there are several series supporting PA as a treatment not associated with additional morbidity when compared with TA [20,21]. Moreover, despite small sample sizes, in two different PA series (for primary aldosteronism and pheochromocytoma) the authors reported absence of ipsilateral recurrences at 16- and 36-mo follow-up, respectively [22,23].

Besides, one study demonstrated that patients with a solitary adrenal gland do not respond "equally well" to stressful situations when compared with normal controls, underscoring the potential role of PA regardless the status of the contralateral gland [24]. Efficacy of adrenal-sparing surgery usually relies on the rate of recurrence and rate of normal adrenal function. However, interpreting functional outcomes of PA can be difficult, due to parity of this gland. Brauckhoff et al [25] suggested that after PA, at least 15–30% of the adrenal tissue in situ is needed to ensure a normal cortical function. Assessment of functional outcomes of paired organs after conservative treatments would require assessment of split function [26]. Notwithstanding, assessment of renal function after PN with serum creatinine and estimated glomerular filtration rate is still the standard practice; similarly, assessment of functional outcomes after adrenal surgery is still performed based on biochemical and clinical parameters, according to PASO criteria (Table 1) [14]. A multidisciplinary team management including endocrinologic preoperative evaluation is essential as in the diagnostic workflow, distinguishing between UAPA and bilateral adrenal hyperplasia, as in the follow-up, to properly assess clinical effects of surgery [11,12,27].

Although TA represents an established treatment for the management of adrenal masses, we believe that main advantages of the robotic approach in the adrenal-sparing surgery are represented by the minimized manipulation of the surrounding adrenal cortex and preservation of blood supply of the adrenal remnant parenchyma, overcoming the technical challenges of laparoscopic surgery. The rationale of avoiding dissection of adrenal vessels and therefore proceeding with an off-clamp approach is strongly supported by the potential risks of injuring the small adrenal vessels and also of serious intraoperative complications such as hypertensive crises, which may have dramatic clinical sequelae.

Notably, the cost of a robotic platform represents a drawback associated with PA [3]. However, we believe that its added value should be considered in technically challenging cases, such as larger-size adenomas, adrenal malignant tumors, or bilateral disease. In this setting, as recently demonstrated for robotic PN, higher costs due to robotic system use could be balanced by a shorter hospital stay, reduced perioperative complications, and potentially improved functional outcomes [28,29].

Our study is not devoid of limitations. We considered an elective partial approach only for patients with small (≤3 cm), solitary, and unilateral adrenal masses. Consequently, our results may not be comparable for more technically demanding cases such as bilateral adrenal masses or complex diseases such as pheochromocytoma or adrenal cancer. Furthermore, the wide robotic experience of surgical teams involved in the study may limit reproducibility outside of referral centers. Additionally, the small sample size, lack of a matched TA cohort, and limited follow-up preclude conclusive messages about PA versus TA.

Eventually, in our preliminary experience, we confirmed feasibility and safety of this technique, reporting excellent functional outcomes with 90% of patients achieving durable biochemical and clinical success rates at a median follow-up of 30 mo.

## 5. Conclusions

RAPA can safely be performed in selected cases with excellent outcomes that appear comparable with those reported for TA. For the time being, the decision to proceed with an adrenal-sparing approach should be based mainly on multidisciplinary team evaluation and technical feasibility.

***Author contributions***: Giuseppe Simone had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

*Study concept and design*: Simone, Celia, Gallucci.
*Acquisition of data*: Tuderti, Anceschi, Costantini, Minisola, Ferriero, De Concilio, Guaglianone, Misuraca, Stigliano.
*Analysis and interpretation of data*: Simone, Tuderti.
*Drafting of the manuscript*: Anceschi, Simone.
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## Appendix A. Supplementary data

The Surgery in Motion video accompanying this article can be found in the online version at https://doi.org/10.1016/j.eururo.2018.07.030 and via www.europeanurology.com.

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