World J Surg (2020) 44:810–818
https://doi.org/10.1007/s00268-019-05287-2

ORIGINAL SCIENTIFIC REPORT

# Are Adrenal Lesions of 6 cm or More in Diameter a Contraindication to Laparoscopic Adrenalectomy? A Case–Control Study

**Andrea Balla[1] · Livia Palmieri[1] · Francesca Meoli[1] · Diletta Corallino[1] · Monica Ortenzi[2] · Pietro Ursi[1] · Mario Guerrieri[2] · Silvia Quaresima[1] · Alessandro M. Paganini[1]**

Published online: 14 November 2019


## Abstract

*Background* The aim of this case–control study is to compare the surgical outcomes of laparoscopic adrenalectomy (LA) for lesions measuring ≥6 cm versus ≤5.9 cm in diameter.

*Methods* Eighty-one patients with adrenal gland lesions ≥6 cm in diameter (intervention group) were identified. Patients were matched to 81 patients with adrenal gland ≤5.9 cm in diameter (control group) based on disease (Conn–Cushing syndrome, pheochromocytoma, primary or secondary adrenal cancer or other disease), lesion side (right, left), surgical technique (anterior transperitoneal approach for right and left LA or anterior transperitoneal submesocolic for left LA) and body mass index class (18–24.9, 25–29.9, 30–34.9, 35–39.9, ≥40 kg/m$^2$). Surgical outcomes were compared between the intervention and control groups.

*Results* Mean operative time was statistically significantly longer in the interventional arm (101.4 ± 52.4 vs. and 85 ± 31.6 min, $p = 0.0174$). Eight conversions were observed in the intervention group (9.8%) compared to four in the control group (4.9%) ($p = 0.3690$). Five (6.1%) and three (3.7%) postoperative complications were observed in the intervention and control groups, respectively ($p = 0.7196$). Mean postoperative hospital stay was 4.6 ± 2.4 and 4.1 ± 2.3 days in the intervention and control groups, respectively ($p = 0.1957$).

*Conclusions* Operative time was statistically significantly longer in adrenal gland lesions ≥6 cm in diameter (vs. ≤5.9 cm). Conversion and complication rates were also higher, but the difference was not statistically significant. Based on the present data, adrenal gland lesions ≥6 cm in diameter are not an absolute contraindication to the laparoscopic approach.

## Introduction

In 1992, Gagner et al. introduced laparoscopic transperitoneal adrenalectomy with the patient positioned in lateral decubitus [1]. Since then, the minimally invasive approach has been widely adopted for the surgical treatment of adrenal gland disease and is now considered the gold standard [2, 3]. Laparoscopic adrenalectomy (LA) is associated with lower morbidity, less blood loss, less postoperative pain and shorter hospital stay, as compared to open surgery [3–5].

The adrenal gland may be approached by the retroperitoneal route with the patient in the prone or lateral

✉ Andrea Balla
andrea.balla@gmail.com

[1] Department of General Surgery and Surgical Specialties "Paride Stefanini", Sapienza University of Rome, Azienda Policlinico Umberto I, Viale del Policlinico 155, 00161 Rome, Italy

[2] Department of General Surgery, Università Politecnica delle Marche, Piazza Roma 22, 60121 Ancona, Italy

decubitus position, and by a transperitoneal route with the patient supine or in lateral decubitus position [6–10]. Currently, the most popular approaches are the lateral transperitoneal and retroperitoneal routes. Purported advantages are a wider working space and more easily identified anatomical landmarks for the former, and less postoperative pain with earlier recovery of bowel function due to the absence of intestinal manipulation, for the latter [6–12]. However, clear advantages of one approach over the other are still missing [10, 13].

The indication for a laparoscopic approach in case of large adrenal lesions is still debated in the literature [2, 12, 14, 15]. While laparoscopy in case of a bulky mass is associated with prolonged operative time, LA offers better postoperative outcomes as compared with an open approach [3–5]. For these reasons, some authors do not consider size to be an absolute contraindication for a minimally invasive approach [12, 14].

The aim of this case–control study is to compare the surgical outcomes in patients undergoing LA with an anterior approach for lesions measuring 6 cm or more versus lesions in which the diameter is smaller.

## Materials and methods

This is a case–control study of prospectively collected data. Informed consent was provided by all participants and institutional review board approval was obtained. From January 1994 to August 2018, 552 LAs were performed in two centers which follow the same diagnostic and treatment protocol and identical surgical approach, as previously reported [8–10, 16]. Patients who underwent bilateral adrenalectomy were excluded from the present study (21 patients).

Out of 531 remaining patients, 81 patients with an adrenal lesion diameter ≥6 cm with no venous tumor thrombus who underwent LA were identified (intervention group) and were paired with 81 patients with adrenal lesion diameter ≤5.9 cm (control group), based on diagnosis (Conn–Cushing syndrome, pheochromocytoma, primary adrenal cancer or metastases, other types of lesions), lesion side (right, left), surgical technique (anterior transperitoneal for both right and left LA or anterior transperitoneal submesocolic for left LA, as published previously [8–10]) and body mass index (BMI) class divided into five subgroups (18–24.9, 25–29.9, 30–34.9, 35–39.9, ≥40 kg/m$^2$) (Fig. 1). Subgroup analysis was performed according to diagnosis [Conn–Cushing syndrome (Group A), pheochromocytoma (Group B), primary adrenal cancer or metastases (Group C), other diseases (Group D)], lesion side, surgical technique and BMI.

### Study design

Data on gender, age, BMI, previous abdominal surgery, surgical approach, lesion size, associated procedures, conversions, operative time, postoperative complications (graded according to the Clavien–Dindo Classification [17]), blood transfusions, postoperative hospital stay and definitive histology were stored in a Microsoft Excel program (Microsoft Corporation, Redmond, Washington, USA).

### Statistical analysis

Surgical outcomes were compared between patients with adrenal gland lesions ≥6 cm in diameter and patients with lesions ≤5.9 cm. For continuous variables, results are expressed as mean ± standard deviation (SD) and for categorical variables as frequencies and percentages. The student *t* test and Fisher's exact test were employed for statistical analysis as appropriate. A *p* value lower than 0.05 was considered statistically significant. Statistical analyses were carried out with SPSS software 22.0 (SPSS Inc., Chicago, Illinois, USA).

## Results

Patient characteristics and surgical outcomes for the entire series are shown in Table 1. Aside from the obvious statistically significant difference in mean lesion size (6.9 ± 1.4 and 3.3 ± 1.1 cm, $p = <0.0001$), mean operative time was statistically significantly longer (101.4 ± 52.4 min and 85 ± 31.6 min, $p = 0.0174$) in the intervention (vs. control) group (Table 1).

Overall, we observed eight conversions to open surgery in the intervention group. Two occurred during left submesocolic adrenalectomy due to: bleeding ($n = 1$) and adhesions from previous surgery ($n = 1$). Six conversions were performed during right adrenalectomy due to: bleeding ($n = 3$), vena cava adhesions ($n = 1$), retrocaval and medial adrenal mass growth ($n = 1$), difficult dissection of the adrenal mass ($n = 1$). Four conversions were necessary in the control group: three during left anterior adrenalectomy (bleeding, adhesions from previous surgery and adhesions to diaphragmatic crura) and one during right adrenalectomy (hepatomegaly). Five postoperative complications were observed in the intervention group, two during left submesocolic adrenalectomy [trocar hematoma (Clavien–Dindo I), fever (Clavien–Dindo II)] and three during right adrenalectomy [wound infection, anemia (Clavien–Dindo II), hemoperitoneum (Clavien–Dindo IIIb)]. In the control group, three postoperative complications were observed: two during left anterior adrenalectomy

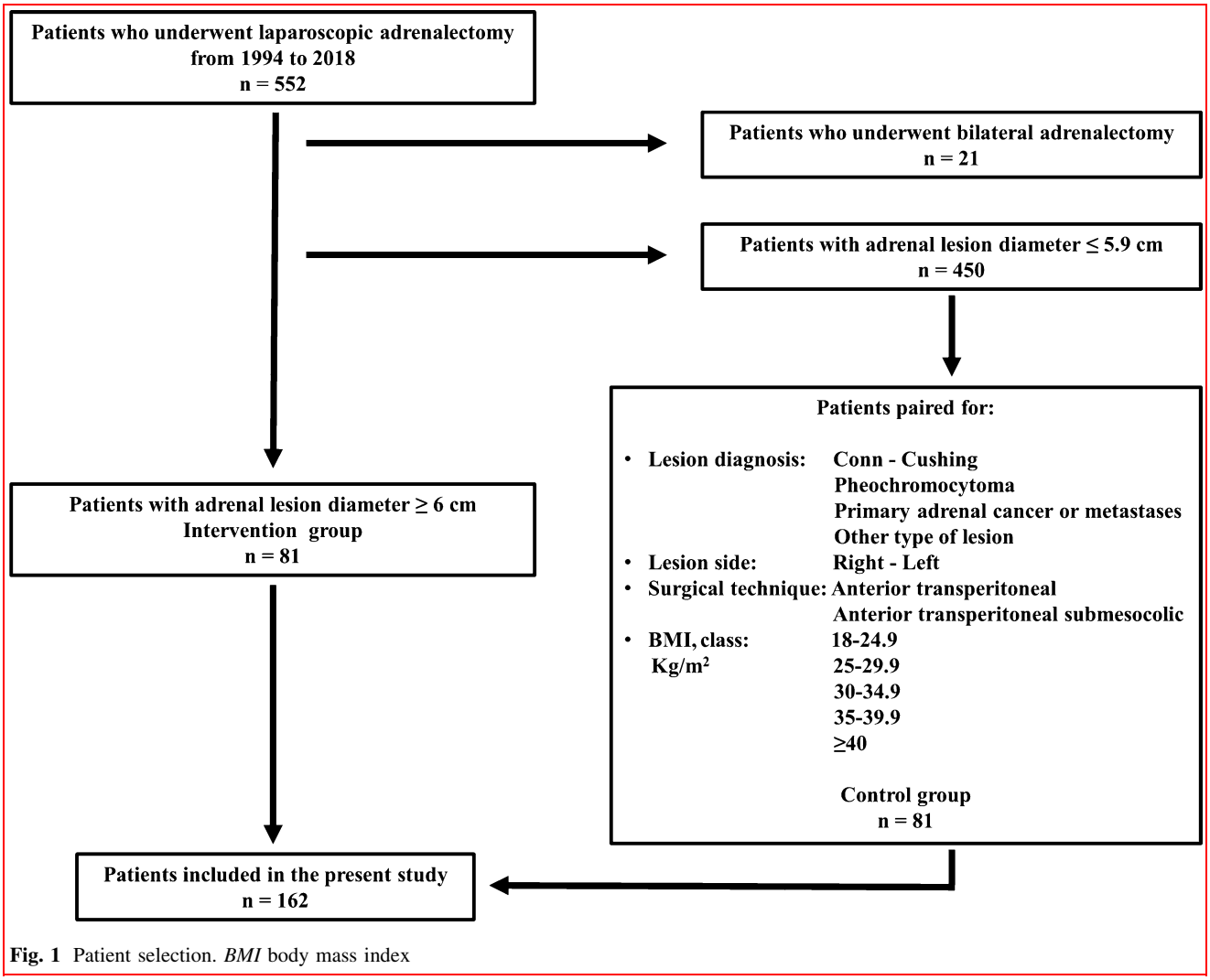


**Fig. 1** Patient selection. *BMI* body mass index

[wound infection (Clavien–Dindo II), chylous ascites (Clavien–Dindo III-a)] and one during right adrenalectomy [wound infection (Clavien–Dindo II)]. Statistically significant differences regarding conversions and complications were not found (Table 1). Mortality was nil.

In subgroup analysis based on diagnosis, 48 patients (24 intervention and 24 control) were included in group A, 46 (23 intervention and 23 control) in group B, 22 (11 intervention and 11 control) in group C and 46 (23 intervention and 23 control) in group D (Tables 1, 2). A statistically significant difference was observed in mean hospital stay for group A only ($p = 0.0392$) (Table 2). With regard to intraoperative and postoperative outcomes among the four control subgroups, statistically significant differences were found in the mean operative time between groups A and D ($p = 0.0327$) and groups C and D ($p = 0.0180$), and in the mean hospital stay between groups A and B ($p = 0.0298$), B and D ($p = 0.0124$), and C and D ($p = 0.0466$). No statistically significant differences were found between the four subgroups in the interventional arm.

In subgroup analysis based on laterality, the operative time was statistically significantly longer for the intervention group in patients with right-sided lesions ($p = 0.0237$) (Table 3). For left-sided lesions, there was no statistically significant difference in outcomes (Table 3), as well as between patients with left-sided versus right-sided lesions. For left LA, mean hospital stay was statistically significantly longer for the submesocolic approach (vs. the control group, $p = 0.0057$) (Table 4). As well, in the control group, the conversion rate ($p = 0.0369$) and mean hospital stay ($p < 0.0001$) were statistically significantly higher and longer, respectively, when the anterior approach was compared with the submesocolic approach (Table 4).

With regard to BMI, the only statistically significant difference between the two groups was in operative time when BMI was between 25 and 29.9 kg/m$^2$ ($p = 0.0102$) (Table 5). Comparing outcomes among the five BMI

**Table 1** Patient characteristics and surgical outcomes

| Group | Indication to surgery | Intervention group $n = 81$ | Control group $n = 81$ | $p$ value |
|---|---|---|---|---|
| A | Conns–Cushing's syndrome, $n$ (%) | 24 (29.6) | 24 (29.6) | 1.0000 |
| | Adenoma | 12 (50) | 12 (50) | 1.0000 |
| | Hyperplasia | 12 (20) | 12 (50) | 1.0000 |
| B | Pheochromocytoma, $n$ (%) | 23 (28.4) | 23 (28.4) | 1.0000 |
| C | Primary cancer or metastases, $n$ (%) | 11 (13.6) | 11 (13.6) | 1.0000 |
| | Primary adrenal carcinoma | 8 (72.7) | 4 (36.4) | 0.1984 |
| | Metastases | 3 (27.3) | 7 (63.4) | 0.1984 |
| | | stomach 1 (9) | lung 2 (18.2) | |
| | | bladder 1 (9) | endometrium 1 (9) | |
| | | biliary-pancreatic 1 (9) | kidney 1 (9) | |
| | | | breast 1 (9) | |
| | | | undifferentiated 1 (9) | |
| | | | squamous 1 (9) | |
| D | Other type of lesion, n (%) | 23 (28.4) | 23 (28.4) | 1.0000 |
| | Myelolipoma | 8 (34.7) | 8 (34.7) | 1.0000 |
| | Non-secreting adenoma | 7 (30.4) | 7 (30.4) | 1.0000 |
| | Non-secreting hyperplasia | 4 (17.4) | 4 (17.4) | 1.0000 |
| | Adrenal cyst | 4 (17.4) | 3 (13) | 1.0000 |
| | Angiomyolipoma | 0 (0) | 1 (4.3) | 1.0000 |
| Sex ratio (M:F) | | 44:37 | 32:49 | 0.0830 |
| Mean age ± SD, years (range) | | 52.2 ±14.7 (20–85) | 53.4 ±14.6 (20–79) | 0.5896 |
| Mean BMI ± SD, kg/m$^2$ (range) | | 26.9 ±5.2 (18.4–41) | 27 ±5.5 (18.5–42) | 0.8993 |
| Previous abdominal surgery, $n$ (%) | | 18 (22.2) | 12 (14.8) | 0.3119 |
| Lesion side (right, left), $n$ (%) | | 35 R (43.2) | 35 R (43.2) | 1.0000 |
| | | 46 L (56.8) | 46 L (56.8) | 1.0000 |
| Mean lesion size ± SD, cm (range) | | 6.9 ± 1.4 (6–12) | 3.3 ± 1.1 (1–5.8) | **<0.0001** |
| Associated procedures, n (%) | | 0 | 0 | 1.0000 |
| Conversion rate, $n$ (%) | | 8 (9.8) | 4 (4.9) | 0.3690 |
| Mean operative time ± SD, minutes (range) | | 101.4 ± 52.4 (30–300) | 85 ± 31.6 (33–190) | **0.0174** |
| Complications, $n$ (%, Clavien–Dindo classification, grade) | | 5 (6.1, 1 I, 3 II, 1 III-b) | 3 (3.7, 2 II, 1 III-a) | 0.7196 |
| Blood transfusions in patients, $n$ (%) | | 4 (4.9) | 0 | 0.1204 |
| Mean hospital stay ± SD, days (range) | | 4.6 ± 2.4 (2–13) | 4.1 ± 2.3 (2–16) | 0.1957 |

Group A: Conn–Cushing syndrome, group B: pheochromocytoma, group C: primary adrenal cancer or metastases, group D: other type of lesion. *BMI* body mass index, *SD* standard deviation. Statistically significant differences in bold

subgroups, statistically significant differences were observed in the mean lesion size between BMI 18–24.9 and 30–34.9 kg/m$^2$ ($p = 0.0127$), and in the mean operative time between BMI 25–29.9 and 30–34.9 kg/m$^2$ ($p = 0.0195$) and between BMI 25–29.9 and ≥40 kg/m$^2$ ($p = 0.0289$) in the intervention group. Statistically significant differences were observed in the conversion rate between BMI 18–24.9 and 30–34.9 kg/m$^2$ ($p = 0.0166$) and between BMI 25–29.9 and 30–34.9 kg/m$^2$ ($p = 0.0166$), and in the mean operative time between BMI 25–29.9 and 30–34.9 kg/m$^2$ ($p = 0.0173$) and between BMI 25–29.9 and ≥40 kg/m$^2$ ($p = 0.0080$), in the control group.

## Discussion

Our study showed that the only statistically significant difference that was observed between patients with adrenal lesions ≥6 cm in diameter and patients with lesions ≤5.9 cm was the mean operative time, longer in case of larger lesions ($p = 0.0174$). Conversions and complication rates occurred more frequently in the intervention group, but this difference was not statistically significant ($p = 0.3690$ and $p = 0.7196$, respectively).

In the present study, we chose to adopt the 6 cm diameter cut-off value because this limit has been used most often in previously published articles [14, 15, 18–22].

**Table 2** Surgical outcomes based on diagnosis

| Group | Operative data | Intervention group $n = 81$ | Control group $n = 81$ | $p$ value |
|---|---|---|---|---|
| A $n = 48$ | Mean lesion size ± SD, cm (range) | 7 ±1.7 (6–12) | 3.4 ± 1.1 (1.3–5.8) | **<0.0001** |
| | Conversion rate, $n$ (%) | 1 (4.1) | 1 (4.1) | 1.0000 |
| | Mean operative time ± SD, minutes (range) | 105.2 ±55.5 (30–250) | 91.3± 34.7 (33–180) | 0.3066 |
| | Complications, $n$ (%, Clavien–Dindo classification, grade) | 1 (4.1, 1 I) | 0 | 1.0000 |
| | Blood transfusions in patients, $n$ (%) | 1 (4.1) | 0 | 1.0000 |
| | Mean hospital stay ± SD, days (range) | 5 ± 2.8 (2–12) | 3.5±1.5 (2–7) | **0.0392** |
| B $n = 46$ | Mean lesion size ± SD, cm (range) | 6.9 ±1.4 (6–12) | 3.2 ±1.3 (1–5) | **<0.0001** |
| | Conversion rate, $n$ (%) | 4 (17.3) | 1 (4.3) | 0.3463 |
| | Mean operative time ± SD, minutes (range) | 101 ± 49.8 (50–240) | 83.7 ± 27.7 (40–135) | 0.1510 |
| | Complications, $n$ (%, Clavien–Dindo classification, grade) | 2 (8.6, 2 II) | 2 (8.6, 1 II, 1 III-a) | 1.0000 |
| | Blood transfusions in patients, $n$ (%) | 2 (8.695) | 0 | 0.4889 |
| | Mean hospital stay ± SD, days (range) | 4.7 ±2.1 (2–9) | 5.3 ± 3.3 (2–16) | 0.5364 |
| C $n = 22$ | Mean lesion size ± SD, cm (range) | 7.2 ± 1.6 (6–11) | 2.8 ± 1 (1–3.6) | **<0.0001** |
| | Conversion rate, $n$ (%) | 0 (0) | 2 (18.1) | 0.4762 |
| | Mean operative time ± SD, minutes (range) | 109.5±69.1 (50–300) | 100±42.8 (50–190) | 0.7011 |
| | Complications, $n$ (%, Clavien–Dindo classification, grade) | 0 | 1 (9, 1 II) | 1.0000 |
| | Blood transfusions in patients, $n$ (%) | 0 | 0 | 1.0000 |
| | Mean hospital stay ± SD, days (range) | 4.4 ± 3 (2–13) | 4.5 ± 2 (2–8) | 0.9355 |
| D $n = 46$ | Mean lesion size ± SD, cm (range) | 6.8 ± 1 (6–10) | 3.4 ± 1 (1.1–5) | **<0.0001** |
| | Conversion rate, $n$ (%) | 3 (13) | 0 | 0.2333 |
| | Mean operative time ± SD, minutes (range) | 93.9±44.7 (45–180) | 72.7± 21.5 (35–120) | 0.0464 |
| | Complications, $n$ (%, Clavien–Dindo classification, grade) | 2 (8.6, 1 II, 1 III-b) | 0 | 0.4889 |
| | Blood transfusions in patients, $n$ (%) | 1 (4.3) | 0 | 1.0000 |
| | Mean hospital stay ± SD, days (range) | 4.1±2 (2–8) | 3.3±1.4 (2–6) | 0.1149 |

Group A: Conn–Cushing syndrome, group B: pheochromocytoma, group C: primary adrenal cancer or metastases, group D: other type of lesion. *SD* standard deviation. Statistically significant differences in bold

In our opinion, the choice of this cut-off value in the literature could be related to the increased risk of intra- or postoperative complications due to the need for more extensive surgical dissection, the increased risk of adrenal cancer and the need of extended incision to extract the specimen. In order to obtain a homogeneous series of patients and to reduce the risk of bias that could have influenced the perioperative outcomes, we decided to pair the patients based on diagnosis, lesion side, surgical technique employed and BMI class. In previously published articles, all patients who underwent LA were included without any paired comparison, thus increasing the risk of selection bias and leading to erroneous interpretation of results [14, 15, 18, 19, 21, 23–26].

The observed difference in mean operative time between the intervention and the control group (101.4 ± 52.4 min and 85 ± 31.6 min, respectively) is similar to previously reported data [14, 15, 19, 21–24]. Natkaniec et al., using the transperitoneal lateral approach, found mean operative time was statistically significantly longer in patients with adrenal lesion diameter ≥6 cm ($n = 89$) compared to patients with adrenal lesion diameter <6 cm ($n = 441$) (111.9 ± 43.7 min vs. 86.6 ± 35 min, respectively, $p = <0.0001$) [15]. Highlighting pheochromocytoma, Chung et al. reported that the lateral retroperitoneal approach required significantly longer operative time for pheochromocytoma >6 cm, compared to pheochromocytomas ≤6 cm [19]. Rao et al., in a retrospective analysis of LA with a transperitoneal lateral approach for pheochromocytoma and using a cut-off value of 4 cm, reported a longer operative time but this difference was not statistically significant [23]. In our study, subgroup analysis based on diagnosis did not show any statistically significant difference between the groups, not even in case of pheochromocytoma. Similarly, no important differences were observed in the comparisons between left and right LA.

Natkaniec et al. reported a statistically significant difference in conversion rates between patients with lesions ≥6 cm vs. < 6 cm in diameter, 6.7% and 0.5%, respectively ($p < 0.0001$) [15]. This contrasts with Hwang et al., who retrospectively analyzed 133 patients using a 5 cm

**Table 3** Surgical outcomes based on side of adrenal lesions

| Side | Operative data | Intervention group $n = 81$ | Control group $n = 81$ | $p$ value |
|---|---|---|---|---|
| Right $n = 35$ | Mean lesion size ± SD, cm (range) | 6.8 ±1.1 (6–12) | 3.4 ±1.1 (1–5) | **<0.0001** |
| | Conversion rate, $n$ (%) | 6 (17.1) | 1 (2.8) | 0.1060 |
| | Mean operative time ± SD, minutes (range) | 100.1 ±45.6 (45–240) | 78.5 ±31 (33–180) | **0.0237** |
| | Complications, $n$ (%, Clavien–Dindo classification, grade) | 3 (8.5, 2 II, 1 III-b) | 1 (2.8, 1 II) | 0.6139 |
| | Blood transfusions in patients, $n$ (%) | 3 (8.5) | 0 | 0.2391 |
| | Mean hospital stay ± SD, days (range) | 4.4 ±2.3 (2–10) | 4.2 ±2.8 (2–16) | 0.7852 |
| Left $n = 46$ | Mean lesion size ± SD, cm (range) | 7 ±1.6 (6–12) | 3.1 ±1.1 (1–5.8) | **<0.0001** |
| | Conversion rate, $n$ (%) | 2 (4.3) | 3 (6.5) | 1.0000 |
| | Mean operative time ± SD, minutes (range) | 102.3 ±57.5 (30–300) | 90 ± 31.5 (35–190) | 0.2038 |
| | Complications, $n$ (%, Clavien–Dindo classification, grade) | 2 (4.3, 1 I, 1 II) | 2 (4.3, 1 II, 1 III a) | 1.0000 |
| | Blood transfusions in patients, $n$ (%) | 1 (2.1) | 0 | 1.0000 |
| | Mean hospital stay ± SD, days (range) | 4.7 ± 2.5 (2–13) | 4 ±1.9 (2–9) | 0.1225 |
| $p$ value | Mean lesion size | 0.3785 | 0.2532 | – |
| | Conversion rate | 0.0707 | 0.6299 | – |
| | Mean operative time | 0.8498 | 0.1081 | – |
| | Complications | 0.6475 | 1.0000 | – |
| | Blood transfusions in patients | 0.3105 | 1.0000 | – |
| | Mean hospital stay | 0.5499 | 0.6619 | – |

*SD* standard deviation. Statistically significant differences in bold

**Table 4** Surgical outcomes based on type of left approach

| Left approach | Operative data | Intervention group $n = 81$ | Control group $n = 81$ | $p$ value |
|---|---|---|---|---|
| Anterior $n = 16$ | Mean lesion size ± SD, cm (range) | 7.9 ± 1.9 (6–11) | 3.3 ±1.1 (1–3.3) | **<0.0001** |
| | Conversion rate, $n$ (%) | 0 | 3 (18.7) | 0.2258 |
| | Mean operative time ± SD, minutes (range) | 122.5±60.1 (55–300) | 98.8±36.5 (60–190) | 0.1897 |
| | Complications, $n$ (%, Clavien–Dindo classification, grade) | 0 | 2 (12.5, 1 II, 1 III-a) | 0.4839 |
| | Blood transfusions in patients, $n$ (%) | 0 | 0 | 1.0000 |
| | Mean hospital stay ± SD, days (range) | 5 ±2.5 (2–13) | 5.6 ±2.1 (2–9) | 0.4614 |
| Submesocolic $n = 30$ | Mean lesion size ± SD, cm (range) | 6.6 ±1.2 (6–12) | 3 ± 1.2 (1.1–5.8) | **<0.0001** |
| | Conversion rate, $n$ (%) | 2 (6.6) | 0 | 0.4915 |
| | Mean operative time ± SD, minutes (range) | 91.6 ±54 (30–250) | 85.2 ± 28.1 (35–160) | 0.5675 |
| | Complications, $n$ (%, Clavien–Dindo classification, grade) | 2 (6.6, 1 I, 1 II) | 0 | 0.4915 |
| | Blood transfusions in patients, $n$ (%) | 1 (3.3) | 0 | 1.0000 |
| | Mean hospital stay ± SD, days (range) | 4.6 ± 2.5 (2–12) | 3.1 ± 1.1 (2–6) | **0.0057** |
| $p$ value | Mean lesion size | **0.0107** | 0.4513 | – |
| | Conversion rate | 0.5362 | **0.0369** | – |
| | Mean operative time | 0.0835 | 0.1665 | – |
| | Complications | 0.5362 | 0.1159 | – |
| | Blood transfusions in patients | 1.0000 | 1.0000 | – |
| | Mean hospital stay | 0.5637 | **0.0001** | – |

*SD* standard deviation. Statistically significant differences in bold

**Table 5** Surgical outcomes based on body mass index

| BMI class (kg/m$^2$) | Operative data | Intervention group $n$ = 81 | Control group $n$ = 81 | $p$ value |
|---|---|---|---|---|
| 18–24.9 $n$ = 32 | Mean lesion size ± SD, cm (range) | 6.8 ± 0.9 (6–9) | 3.2 ± 1.1(1–5) | **<0.0001** |
| | Conversion rate, $n$ (%) | 3 (9.4) | 0 | 0.2407 |
| | Mean operative time ± SD, minutes (range) | 92.7 ± 39.8 (50–190) | 83.7 ± 31.6 (35–160) | 0.3219 |
| | Complications, $n$ (%, Clavien–Dindo classification, grade) | 4 (12.5) 3 II, 1 I | 1 (3.1) III-a | 0.3547 |
| | Blood transfusions in patients, $n$ (%) | 2 (6.3) | 0 | 0.4938 |
| | Mean hospital stay ± SD, days (range) | 4.4 ± 2.2 (2–10) | 3.8 ± 1.8 (2–9) | 0.1787 |
| 25–29.9 $n$ = 32 | Mean lesion size ± SD, cm (range) | 7 ± 1.7 (6–12) | 3.5 ± 1.2 (1.1–5) | **<0.0001** |
| | Conversion rate, $n$ (%) | 4 (12.5) | 0 | 0.1132 |
| | Mean operative time ± SD, minutes (range) | 109 ± 64 (45–300) | 77.1 ± 22.6 (33–125) | **0.0102** |
| | Complications, $n$ (%, Clavien–Dindo classification, grade) | 1 (3.1) III-b | 1 (3.1) II | 1.0000 |
| | Blood transfusions in patients, $n$ (%) | 1 (3.1) | 0 | 1.0000 |
| | Mean hospital stay ± SD, days (range) | 4 ± 2 (2–9) | 3.8 ± 2.2 (2–12) | 0.7250 |
| 30–34.9 $n$ = 12 | Mean lesion size ± SD, cm (range) | 7.6 ± 2 (6–11) | 3.1 ± 1.1 (1–4.6) | **<0.0001** |
| | Conversion rate, $n$ (%) | 1 (8.3) | 3 (25) | 0.5901 |
| | Mean operative time ± SD, minutes (range) | 96.3 ± 41.7 (30–180) | 102.1 ± 44.1 (55–190) | 0.7424 |
| | Complications, $n$ | 0 | 0 | 1.0000 |
| | Blood transfusions in patients, $n$ (%) | 1 (8.3) | 0 | 1.0000 |
| | Mean hospital stay ± SD, days (range) | 6 ± 3.1 (2–13) | 5.4 ± 3.7 (2–16) | 0.6787 |
| 35–39.9 $n$ = 1 | Mean lesion size ± SD, cm (range) | 6 | 2.5 | – |
| | Conversion rate, $n$ (%) | 0 | 0 | 1.0000 |
| | Mean operative time ± SD, minutes (range) | 135 | 70 | – |
| | Complications, $n$ | 0 | 0 | 1.0000 |
| | Blood transfusions in patients, $n$ (%) | 0 | 0 | 1.0000 |
| | Mean hospital stay ± SD, days (range) | 3 | 6 | – |
| ≥40 $n$ = 4 | Mean lesion size ± SD, cm (range) | 7 ± 0.8 (6–8) | 3.5 ± 1.9 (1.3–5) | **0.0063** |
| | Conversion rate, n (%) | 0 | 1 (25) | 1.0000 |
| | Mean operative time ± SD, minutes (range) | 118.8 ± 77 (50–210) | 112.5 ± 32.8 (85–160) | 0.8862 |
| | Complications, $n$ (%, Clavien–Dindo classification, grade) | 0 | 1 (25) II | 1.0000 |
| | Blood transfusions in patients, $n$ (%) | 0 | 0 | 1.0000 |
| | Mean hospital stay ± SD, days (range) | 6.8 ± 3.6 (4–12) | 4.8 ± 2.8 (2–8) | 0.4110 |

*BMI* body mass index, *SD* standard deviation. Statistically significant differences in bold

cut-off value adrenal lesion size [24], and Carter et al. in their series of 26 pheochromocytoma patients using a cut-off value size of 6 cm [18] where no conversion to open surgery was reported. However, in our study, conversion rates of 9.8% and 4.9% were observed in the intervention and control groups, respectively; this difference, however, was not statistically significant ($p$ = 0.3690). The reasons for these discrepancies are that large adrenal masses bleed more easily than smaller lesions; in fact four out of eight conversions in the intervention group were caused by bleeding. Moreover, at right-sided lesions, retrocaval adrenal gland growth can complicate dissection especially with the anterior approach. To the contrary, dissection with patient in lateral decubitus allows to directly visualize the retrocaval space. This might explain why six out of eight conversions were necessary during right adrenalectomy.

In terms of postoperative morbidity, Natkaniec et al. reported a higher complication rate in patients with lesions ≥6 cm (15.7%) compared to patients with lesions <6 cm (9.3%), with a trend toward statistical significance ($p$ = 0.0692) [15]. Hobart et al. reported complication rates of 21.4% and 8.9%, respectively ($p$ = 0.21) in a series of 14 patients [12] similar to our findings ($p$ = 0.7196).

In accordance to others [18, 24], we found no statistically significant difference in mean hospital stay between the two groups ($p$ = 0.1957). However, in contrast, Chen et al. found a statistically significant difference (7.43 days vs. 2.07 days, $p$ = 0.001) in their observational study for

patients with adrenal gland lesions measuring more or less than 5 cm, respectively [25].

Worldwide, most surgeons use the transperitoneal approach with patients positioned in lateral decubitus and the retroperitoneal approach with patients in the prone position [10, 13]. We prefer the anterior transperitoneal approach for right adrenalectomy and the anterior transperitoneal submesocolic approach for left adrenalectomy with patients positioned in the supine position [8–10]. To the best of our knowledge, the anterior approach is performed in very few centers around the world [9, 27–31]. This is in agreement with the lack of a clear superiority of one approach over the other in the literature [8–10, 13, 32], and the recommendations of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) that suggest the surgeon should employ the surgical approach for LA with which he or she is most familiar [13].

Our study has several limitations including its retrospective nature, the lack of control groups with another approach (lateral or retroperitoneal) and the limited number of patients in each group that might have affected the statistical significance.

In conclusion, based on the present study, an adrenal gland lesion of 6 centimeters or more with no venous tumor thrombus is not a contraindication for a laparoscopic management, even in case of pheochromocytoma, provided the necessary experience in LA is present. Further prospective studies with a larger sample size and control groups based also on other minimally invasive approaches are necessary to confirm these data.

**Funding** There are no grant support or financial relationships for the present study.

**Compliance with ethical standards**

**Conflict of interest** Dr. Andrea Balla, Dr. Livia Palmieri, Dr. Francesca Meoli, Dr. Diletta Corallino, Dr. Monica Ortenzi, Dr. Pietro Ursi, Prof. Mario Guerrieri, Dr. Silvia Quaresima and Prof. Alessandro M. Paganini have no conflicts of interest or financial ties to disclose.

**Human and animal rights** The present study was approved by our Institutional review board.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

## References

1. Gagner M, Lacroix A, Bolté E (1992) Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. N Engl J Med 327(14):1033
2. Dalvi AN, Thapar PM, Thapar VB et al (2012) Laparoscopic adrenalectomy for large tumours: single team experience. J Minim Access Surg 8(4):125–128. https://doi.org/10.4103/0972-9941.103110
3. Arora E, Bhandarwar A, Wagh A et al (2018) Role of indocyanine green (ICG) fluorescence in laparoscopic adrenalectomy: a retrospective review of 55 Cases. Surg Endosc 32(11):4649–4657. https://doi.org/10.1007/s00464-018-6309-7
4. Jacobs JK, Goldstein RE, Geer RJ (1997) Laparoscopic adrenalectomy. A new standard of care. Ann Surg 225(5):495–501 **(discussion 501–502)**
5. Guazzoni G, Montorsi F, Bocciardi A et al (1995) Transperitoneal laparoscopic versus open adrenalectomy for benign hyperfunctioning adrenal tumors: a comparative study. J Urol 153(5):1597–1600
6. Coste T, Caiazzo R, Torres F et al (2017) Laparoscopic adrenalectomy by transabdominal lateral approach: 20 years of experience. Surg Endosc 31(7):2743–2751. https://doi.org/10.1007/s00464-016-4830-0
7. Sho S, Yeh MW, Li N et al (2017) Single-incision retroperitoneoscopic adrenalectomy: a North American experience. Surg Endosc 31(7):3014–3019. https://doi.org/10.1007/s00464-016-5325-8
8. Paganini AM, Balla A, Guerrieri M et al (2014) Laparoscopic transperitoneal anterior adrenalectomy in pheochromocytoma: experience in 62 patients. Surg Endosc 28(9):2683–2689. https://doi.org/10.1007/s00464-014-3528-4
9. Paganini AM, Guerrieri M, Balla A et al (2016) Management of adrenal incidentaloma by laparoscopic transperitoneal anterior and submesocolic approach. Langenbecks Arch Surg 401(1):71–79. https://doi.org/10.1007/s00423-015-1367-y
10. Balla A, Quaresima S, Palmieri L et al (2018) Is laparoscopic left adrenalectomy with the anterior submesocolic approach for Conn's or Cushing's syndrome equally safe and effective as the lateral and anterior ones? Surg Endosc. https://doi.org/10.1007/s00464-018-6601-6
11. Mohammadi-Fallah MR, Mehdizadeh A, Badalzadeh A et al (2013) Comparison of transperitoneal versus retroperitoneal laparoscopic adrenalectomy in a prospective randomized study. J Laparoendosc Adv Surg Tech A 23(4):362–366. https://doi.org/10.1089/lap.2012.0301
12. Hobart MG, Gill IS, Schweizer D et al (2000) Laparoscopic adrenalectomy for large-volume (> or = 5 cm) adrenal masses. J Endourol 14(2):149–154
13. Stefanidis D, Goldfarb M, Kercher KW et al (2013) SAGES guidelines for minimally invasive treatment of adrenal pathology. Surg Endosc 27(11):3960–3980. https://doi.org/10.1007/s00464-013-3169-z
14. MacGillivray DC, Whalen GF, Malchoff CD et al (2002) Laparoscopic resection of large adrenal tumors. Ann Surg Oncol 9(5):480–485
15. Natkaniec M, Pędziwiatr M, Wierdak M et al (2016) Laparoscopic transperitoneal lateral adrenalectomy for large adrenal tumors. Urol Int 97(2):165–172. https://doi.org/10.1159/000444146
16. Ortenzi M, Balla A, Ghiselli R et al (2019) Minimally invasive approach to the adrenal gland in obese patients with Cushing's syndrome. Minim Invasive Ther Allied Technol 19:1–7. https://doi.org/10.1080/13645706.2018.1536669
17. Clavien PA, Barkun J, de Oliveira ML et al (2009) The Clavien–Dindo classification of surgical complications: five-year experience. Ann Surg 250(2):187–196
18. Carter YM, Mazeh H, Sippel RS et al (2012) Safety and feasibility of laparoscopic resection for large (≥ 6 CM) pheochromocytomas without suspected malignancy. Endocr Pract 18(5):720–726. https://doi.org/10.4158/EP12014.OR

19. Chung HS, Kim MS, Yu HS et al (2018) Laparoscopic adrenalectomy using the lateral retroperitoneal approach: is it a safe and feasible treatment option for pheochromocytomas larger than 6 cm? Int J Urol 25(5):414–419. https://doi.org/10.1111/iju.13524
20. Agrusa A, Romano G, Frazzetta G et al (2014) Laparoscopic adrenalectomy for large adrenal masses: single team experience. Int J Surg 12(Suppl 1):S72–S74. https://doi.org/10.1016/j.ijsu.2014.05.050
21. Walz MK, Petersenn S, Koch JA, Mann K, Neumann HP, Schmid KW (2005) Endoscopic treatment of large primary adrenal tumours. Br J Surg 92(6):719–723
22. Kercher KW, Novitsky YW, Park A et al (2005) Laparoscopic curative resection of pheochromocytomas. Ann Surg 241(6):919–926 **(discussion 926–928)**
23. Rao N, Ramachandran R, Tandon N et al (2016) Laparoscopic adrenalectomy for pheochromocytoma-does size matter? A single surgeon comparative study. Transl Androl Urol 5(5):780–783
24. Hwang I, Jung SI, Yu SH et al (2014) Is larger tumor size a contraindication to retroperitoneal laparoscopic adrenalectomy? World J Urol 32(3):723–728. https://doi.org/10.1007/s00345-013-1139-7
25. Chen W, Liang Y, Lin W et al (2018) Surgical management of large adrenal tumors: impact of different laparoscopic approaches and resection methods on perioperative and long-term outcomes. BMC Urol 18(1):31. https://doi.org/10.1186/s12894-018-0349-0
26. Zografos GN, Farfaras A, Vasiliadis G et al (2010) Laparoscopic resection of large adrenal tumors. JSLS 14(3):364–368. https://doi.org/10.4293/108680810X12924466007160
27. Linos DA, Stylopoulos N, Boukis M et al (1997) Anterior, posterior, or laparoscopic approach for the management of adrenal diseases? Am J Surg 173(2):120–125
28. Matsuda T, Murota T, Kawakita M (2000) Transperitoneal anterior laparoscopic adrenalectomy: the easiest technique. Biomed Pharmacother 54(Suppl 1):157s–160s
29. Kokorak L, Soltes M, Vladovic P et al (2016) Laparoscopic left and right adrenalectomy from an anterior approach—is there any difference? Outcomes in 176 consecutive patients. Wideochir Inne Tech Maloinwazyjne 11(4):268–273. https://doi.org/10.5114/wiitm.2016.64767
30. Molnar C, Lata L, Pisica R et al (2017) Anterior transabdominal laparoscopic adrenalectomy, without ligatures, for a symptomatic right adrenal myelolipoma with intratumoral hemorrhage. Chirurgia (Bucur) 112(1):58–62. https://doi.org/10.21614/chirurgia.112.1.58
31. Balla A, Ortenzi M, Palmieri L et al (2019) Laparoscopic bilateral anterior transperitoneal adrenalectomy: 24 years experience. Surg Endosc. https://doi.org/10.1007/s00464-019-06665-6
32. Constantinides VA, Christakis I, Touska P et al (2012) Systematic review and meta-analysis of retroperitoneoscopic versus laparoscopic adrenalectomy. Br J Surg 99(12):1639–1648. https://doi.org/10.1002/bjs.8921