Laparoscopic adrenalectomy for giant adrenal tumours: Technical considerations and surgical outcome

Alessio Giordano, Giovanni Alemanno, Carlo Bergamini, Andrea Valeri, Paolo Prosperi
Department of Emergency, Emergency Surgery Unit, Careggi University Hospital, Florence, Italy

INTRODUCTION

Laparoscopic adrenalectomy (LA) is actually considered the gold standard for the treatment for benign adrenal tumours. Since the first description performed by Gagner et al. in 1992,[1] some retrospective studies have confirmed that laparoscopic approach is associated with a decrease of the perioperative morbidity, lower complication rates, less operative blood loss, less post-operative pain and shorter hospital stay compared with open approach. Incidental adrenal tumours are relatively common, and adrenalectomy represents the third most commonly performed endocrine surgical procedure.[2] In literature,
giant adrenal tumours (GAT) are defined as adrenal masses larger than 6 cm.[3] The overall incidence of adrenal tumours that require resection is exceedingly low and for this reason, GAT are considered rare, with an incidence ranging from 8.6% to 38.6% of all adrenal tumours.[4] In large adrenal tumour, it is detriment an accurate pre-operative study to assess the eventual malignancy of the lesion. Laparoscopy in case of GAT requires an accurate dissection to avoid capsular disruption, especially in case of malignancy. The incidence of malignancy in patients with GAT ranges from 10% to 53% with a consensus of 25%,[5] however, there are no evidence that suggests that a laparoscopic approach is contraindicated for GAT because the size is only a predictor factor of malignancy.[6] In this article, we report a 10 years’ experience of LA for GAT.

**PATIENTS AND METHODS**

In our general and emergency surgery unit, between January 2008 and December 2018, 245 patients underwent surgery for adrenal tumour. Among these patients, 50 (20.4%) had GAT (with an adrenal mass larger than 6 cm). Demographic data were retrospectively collected from medical records.

**Pre-operative evaluation**

A multidisciplinary pre-operative study of all adrenal masses, especially of GAT, is mandatory. All patients were assessed by an accurate clinical evaluation, a hormonal assessment and an anatomical and functional imaging. To define the characteristics and size of the lesions, all patients were preoperatively submitted to abdominal magnetic resonance imaging or computed tomography (CT) scan. The only size of the lesion was not considered as a signal of malignant lesion.[7] The diagnosis of possible adrenal carcinoma was based, in fact, on the patient’s history and radiologic findings as local infiltration, irregular margins or tumour heterogeneity, vascular invasion. In cases suspected for pheochromocytoma metaiodobenzylguanidine scintigraphy or positron emission tomography with FDOPA –CT scan (6-[18F]-L-fluoro-L-3, 4-dihydroxyphenylalanine) were performed. Complete hormonal tests were performed to identify functioning tumours. All patients with a pre-operative diagnosis of pheochromocytoma received specific pre-operative preparation. Indications for adrenalectomy included: hormone-secreting tumours (Cushing’s lesion, aldosteronoma and pheochromocytomas) and all non-functioning tumours >4 cm.[8]

**Surgical technique**

All surgical operations were performed at our care centre unit by experienced laparoscopic surgeons in adrenal surgery. Laparoscopic adrenalectomies were performed using the lateral transperitoneal approach. Patients were placed in a lateral decubitus position with the affected side up. This approach allows a wider surgical workspace with an excellent exposure of the upper retroperitoneum, good control of vascular structure if compared to other approaches.[9] For the right adrenalectomy, we used four trocars in the right subcostal region, instead, for left-sided resection, we used three trocars in the left subcostal region. On the left-sided adrenalectomy, we used always fibrin glue for repositioning splenic-pancreatic block. One drainage was routinely used in all operations. At the end of the procedure, the large tumours were positioned in endobag device and removed with a subcostal mini-laparotomy. During the procedures, all tumours were handled with care, especially in cases of pheochromocytoma or carcinoma. No retroperitoneoscopic approach was performed. Open adrenalectomy (OA), with a transabdominal approach, was performed in cases with radiological findings of local invasion of the periadrenal fat tissue. Figure 1 shows a case of giant adrenal carcinoma removed with a laparoscopic approach.

**Post-operative evaluation**

All patients were transferred to a recovery room for the first 4–6 h after surgery, to monitor their blood pressure. The Clavien-Dindo system was used for grading complications which occur as a result of surgical procedures.

**Follow-up**

Patients were checked in our outpatient clinic 1 week after the discharge. The follow-up protocol included the possibility of an on-call activation of our surgical team in case of adverse abdominal symptoms.
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Statistical analysis
Data were expressed as a mean ± standard deviation. Statistical analyses were performed with the Chi-square test, Fisher’s exact test or t-test. Statistical significance was set at P < 0.05, and resulting P values were adjusted according to the Bonferroni correction method. Data were analysed using the SPSS statistical software, IBM® (New York, United States).

Compliance with ethical standards
This retrospective study is in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

RESULTS

In the period of the study, between January 2008 and December 2018, 50 (20.4%) out of 245 patients referred to our centre for adrenal tumours presented with GAT. Thirty-four of these patients (68%) were submitted to LA, and 16 (32%) were submitted to OA. The population of the study was characterised by 28 males and 22 females with a mean age of 57 years (range: 21–81 years). For 24 patients (48%), the GAT was found incidentally, however, other clinical presentation included hypertension, abdominal pain or oncological work-up. Twenty-four patients (48%) presented with a functioning tumours, in particular, 15-secreting catecholamines (62.5%), 6 cortisol (25%), 2 aldosterone (8.3%) and 1 androgen (4.2%). The general characteristics of the population of the study are reported in Table 1.

OA was indicated due to radiological characteristics or suspicion of local invasion (seven cases). In particular, during OA, it was necessary to remove ipsilateral kidney in four patients, spleen with pancreatic tail in one patient and lateral patches of the inferior vena cava in two patients due to local invasion. Whatever type of resection, the mean operative time was longer by an open approach (170 min, range: 140–200 min) than by laparoscopy (110 min, range: 75–130 min) (P = 0.043). Two of 34 patients submitted to LA were converted to OA: one for tenacious adhesions on the right side and one for important bleeding from inferior vena cava. A previous abdominal surgery was not an absolute contraindication for an LA. In all patients submitted to surgery for GAT, the tumour was excised through en bloc resection, and there was no capsular disruption during dissection.

The mean tumour size was 9.9 cm (range: 7–22 cm), and the lesions were localised on the right side in 24 patients and on the left side in 26 patients. We did not observe bilateral adrenal masses. The mean blood loss was 90 ml (range: 60–185 ml) for LA versus 210 ml for OA (range: 170–520 ml), (P = 0.037). The mean post-operative hospital stay for LA was 3 days (range: 2–5 days) versus 7 days (range: 5–14 days) for OA (P = 0.039). In the LA group, we did not observe any post-operative complication, whereas in the OA group, we have observed pulmonary infection in one patient, atrial fibrillation pharmacologically treated in one patient and post-operative anaemia that required blood transfusion in one patient (P = 0.082), as reported in Table 2. We did not observe any cases of major complications required surgical, radiological or endoscopic intervention (Dindo III); life-threatening complications required intensive care (Dindo IV) or death (Dindo V).

Twenty-seven tumours (54%) were malignant (15/34 LA treatment and 12/16 OA treatment), particularly 17 were adrenal carcinoma (34%), five were adrenal metastasis secondary to lung and breast cancer (10%), four were pheochromocytomas (8%) and one was a lymphoma (2%). Benign GATs (46%) included five adenomas (10%), 11 benign pheochromocytomas (22%),

Table 1: General characteristics of 50 patients with giant adrenal tumours

| General characteristics | Characteristics of population of the study |
|-------------------------|------------------------------------------|
| Patients (n)            | 50                                       |
| Male                    | 28                                       |
| Female                  | 22                                       |
| Mean age (years) (range)| 57 (21-81)                               |
| Tumour side, n (%)      |                                          |
| Left side               | 26 (52)                                  |
| Right side              | 24 (48)                                  |
| BMI (kg/m²)             | 25.3±3.5                                 |
| ASA score               |                                          |
| 1                       | 19                                       |
| 2                       | 26                                       |
| 3                       | 5                                        |
| 4                       | 0                                        |
| Surgical approach, n (%)|                                          |
| LA                      | 34 (68)                                  |
| OA                      | 16 (32)                                  |
| Mean tumour size, cm (range) | 9.9 (7-22)                      |
| Functioning tumours, n (%) | 24 (48)                       |
| No functioning tumours, n (%) | 26 (52)                       |

BMI: Body mass index, ASA: American Society of Anaesthesiologists, LA: Laparoscopic adrenalectomy, OA: Open adrenalectomy

Table 2: Results of laparoscopic adrenalectomy versus open approach

|                         | LA (n=34; 68%) | OA (n=16; 32%) | P    |
|-------------------------|----------------|---------------|------|
| Mean blood loss, ml (range) | 90 (60-185)   | 210 (170-520) | 0.037|
| Mean operative time, min (range) | 110 (75-130) | 170 (140-200) | 0.043|
| Hospital stay, days (range) | 3 (2-5)       | 7 (5-14)      | 0.039|
| Post-operative complication (n) | 0             | 3             | 0.082|

LA: Laparoscopic adrenalectomy, OA: Open adrenalectomy
The median follow-up for malignant GAT was about 30 months (range: 6–48 months). No local recurrence and portside metastasis were noticed.

**DISCUSSION**

LA is today considered as the gold standard treatment for benign adrenal tumours. Since the first description in 1992 by Gagner et al., there has been a radical change in the management of adrenal masses because minimally invasive adrenalectomy has been shown to decrease the length of hospital stay, reduce health-care cost, reduce wound complications and blood loss and improve the patient's outcome with an earlier patient mobility and faster return to regular activity. The literature defines the GAT adrenal masses larger than 6 cm, GAT are considered rare, with an incidence ranging from 8.6% to 38.6% of all adrenal tumours. The size criteria remain, at the moment, the subject discussed in literature for the main surgical approach. The size is an important variable in predicting malignancy, in fact, if the lesions are smaller than 4 cm, the risk of malignancy is approximately 2%, whereas for lesions of 4–6 cm, the risk of malignancy is 6%, and for lesions of 6 cm, the risk of malignancy is 25% (10%–53%). At the moment, there are no evidence that suggest that a laparoscopic approach is contraindicated for GAT because the size is only a predictor factor of malignancy. Conversely, the open approach is recommended in patients with evidence at pre-operative imaging studies of malignancy with local invasion of adjacent structures, thus facilitating lymph node dissection and en bloc resection of adjacent structures to achieve negative margins. An incomplete resection or capsular disruption increase the risk of local recurrence and intra-abdominal neoplastic dissemination. It is mandatory to consider that surgeon experience, hospital volume and a multidisciplinary approach, which comprises surgeons, anaesthesiologists and endocrinologists, are three important parameters in the selection of such patients. Over the 10-year study, 50 (20.4%) out of 245 patients referred for adrenal tumours presented with GAT. Thirty-four of these patients (68%) were submitted to LA, 16 (32%) were submitted to OA. LA was technically safe and feasible. The surgical outcome of these patients, compared to OA patients, was better in terms of blood loss, hospital stay and operative time. No statistically differences were registered in terms of post-operative complication.

Laparoscopic adrenalectomies were performed using lateral transperitoneal approach. The lateral transabdominal approach is actually, the most widely practised since it provides a good exposure of the adrenal gland and surrounding structures and provides to surgeon precise anatomic landmark with a safe control to vascular structures. Moreover, it allows to treat other abdominal pathologies simultaneously.

We have drawn up a set of technical caveats with 10 points to follow in all laparoscopic adrenalectomies, and in particular, for the treatment of GAT, based on laparoscopic adrenalectomy experience of our surgical centre [Table 3]. It is fundamental to mention the adequate position of the patient and the trocars to research the correct anatomic landmarks and the main adrenal vein; to avoid the breakdown of the adrenal capsule which would require conversion and to avoid the excessive manipulation of the tumour, in particular in presence of malignance GATs or pheochromocytomas moreover, GATs present a rich vascularisation, particularly observed in cases of pheochromocytoma and metastasis, and for this reasons, the use of clips and radiofrequency scalpel is mandatory. The anomalous adrenal vein anatomy has been described between 9% and 22%, in particular on the left adrenal gland.

Therefore, the LA offers significant advantages compared to open approach. The size of the tumour is not a contraindication to laparoscopy but is only a predictive factor of malignancy. Local ablative therapy is a safe and feasible in terms of surgical and oncological outcome if performed by an experienced laparoscopic surgeon and in high-volume centres. It is necessary to select the patients with GAT through an adequate pre-operative multidisciplinary study. The presence of radiological signs suggestive for malignancy such as vascular infiltration or of the adjacent organs is a contraindication to laparoscopy.

**CONCLUSION**

LA offers significant advantages compared to open approach. The size of the tumour is not a contraindication to laparoscopy but is only a predictive factor of malignancy.

| Table 3: The ‘10 points’ to follow in all laparoscopic adrenalectomies |
|---------------------------------------------------------------|
| 1. Adequate position of patients and trocars                  |
| 2. Using radiofrequency scalpel                              |
| 3. Adequate access to adrenal gland                          |
| 4. Research of the main adrenal vein                         |
| 5. Avoid the breakdown of the adrenal capsule                |
| 6. Avoid excessive manipulation of the tumour                |
| 7. Remove all adipose tissue of adrenal space                 |
| 8. Good control of haemostasis                                |
| 9. Repositioning splenic-pancreatic block on the left side    |
| 10. One drainage                                               |
Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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