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Review

Minimally invasive approach for adrenal lesions: Systematic review of laparoscopic versus retroperitoneoscopic adrenalectomy and assessment of risk factors for complications

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ABSTRACT

In the last decades, minimally invasive transperitoneal laparoscopic adrenalectomy has become the standard of care for surgical resection of the adrenal gland tumors. Recently, however, adrenalectomy by a mininvasive retroperitoneal approach has reached increasingly popularity as alternative technique. Short hospitalization, lower postoperative pain and decrease of complications and a better cosmetic resolution are the main advantages of these innovative techniques. In order to determine the better surgical management of adrenal neoplasms, the Authors analyzed and compared the feasibility and the postoperative complications of minimally invasive adrenalectomy approaches. A systematic research of the English literature, including major meta-analysis articles, clinical randomized trials, retrospective studies and systematic reviews was performed, comparing laparoscopic transperitoneal adrenalectomy versus retroperitoneoscopic adrenalectomy. Many studies support that posterior retroperitoneal adrenalectomy is superior or at least comparable to laparoscopic transperitoneal adrenalectomy in operation time, pain score, blood loss, hospitalization, complications rates and return to normal activity. However, laparoscopic transperitoneal adrenalectomy is up to now a safe and standardized procedure with a shorter learning curve and a similar low morbidity rate, even for tumors larger than 6 cm. Nevertheless, further studies are needed to objectively evaluate these techniques, excluding selection bias and bias related to differences in surgeons' experiences with this approaches.

1. Introduction

Since the first adrenalectomy performed by the English surgeon Thornton in 1889, only in these last decades thanks to improvement of endocrinology knowledge, a better diagnostic support, and especially to minimally invasive techniques, the adrenal surgery has seen an important step forward. The first successful laparoscopic transperitoneal adrenalectomy (LTA) was performed by Michel Gagner in 1992 [1]. Initially adopted to treat small benign tumors, nowadays it is considered the "gold standard" technique to treat a broad spectrum of functioning and non-functioning adrenal diseases with described cases of resection of masses up to 12–15 cm [2–6]. Currently indications to LTA for lesions >6 cm is still a matter of debate and experienced endocrine surgeons are divided between supporters [7–11] and detractors [12,13]. This safe and effective approach offers all the benefits of minimally invasive technique such as low morbidity rate, short hospitalization, improved cosmesis and a rapid recovery in addition to increasing patients' satisfaction and comfort [14]. Shortly after Gagner, Gaur et al. described an alternative minimally invasive technique, the

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retroperitoneoscopic adrenalectomy (RA) [15,16]. This approach consists of two surgical variants, either a posterolateral or a true posterior approach [17–19]. Posterior retroperitoneoscopic adrenalectomy (PRA), was first popularized by Waltz et al., in 1996, and since the beginning appeared resulting in less postoperative pain and a faster recovery than LTA [20–24]. Despite an almost nonexistent mortality, minimally invasive adrenalectomy is still associated with complications rates ranging from 3 to 20% [2,7,25–28]. Advocates for the laparoscopic and retroperitoneoscopic approaches cite the advantage of each technique, but there is no published evidence that supports the superiority of one over the other. Most of the published literature is retrospective, with inadequate or no controls and with potential biases. The aim of this study was to perform a systematic review of English literature, comparing the intraoperative and postoperative complications of the LTA versus RA to identify whether one technique is superior.

2. Surgical technique

2.1. Laparoscopic transperitoneal adrenalectomy

According to Gagner, LTA is performed with patient in lateral decubitus position with the affected side facing upward and the operative table flexed just above the level of the iliac crest [1]. Can be used 3 ports for left-sided tumors, with one additional port if required, and 4 ports for right-sided tumors. The ports are commonly made at the umbilicus and the subcostal area in the anterior axillary and midclavicular lines, port sites could be modified at the discretion of the surgeon. The intra-abdominal pressure is kept at 12 mmHg. For left adrenalectomy, the left colonic flexure is mobilized along to Gerota fascia. Dissecting through the avascular plain between the pancreatic tail and the kidney, the spleen and the pancreatic tail are moved medially. In right adrenalectomy, the liver is mobilized along the lateral border of the inferior vena cava to control potential bleeding. Subsequently, the adrenal vein is identified and divided. The adrenal gland and the surrounding fat tissue are removed en bloc with a retrieval bag.

2.2. Retroperitoneoscopic adrenalectomy

According to Waltz, RA is performed with the patient in a prone jack-knife position, the back prepped and dropped, or in lateral decubitus position (flexed through the torso at a 45° angle), with the surgeon and assistant stand on the side of the operating adrenal gland [20]. The retroperitoneal space is entered posteriorly through a 12 mm transverse incision near to the tip of the 12th rib. A medial 10 mm trocar is placed along the border of the paraspinal muscle at a 45-degree angle pointing directly at the adrenal gland. A lateral 5 mm trocar is placed at the tip of the 11th rib. A 12 mm blunt balloon trocar is then introduced through the initial incision and CO_2 insufflation is established at a pressure of 25 mmHg. The dissection of the retroperitoneal fat tissue from the capsule at the upper renal pole is performed. After visualization of the inferior vena cava at the right side and the identification of the renal vein at the left side, the adrenal vein is divided. Subsequently, dorsal, lateral and cranial mobilization of the tumor is performed. The adrenal gland and the surrounding fat tissue are removed en bloc with a retrieval bag.

2.3. Classification of complication in adrenalectomy

Despite the low morbidity of rate of adrenalectomy, several and severe perioperative complications can occur and they can be classified into intraoperative and postoperative. The most frequent intraoperative complications are bleeding from adrenal and renal vein or adrenal cortex, vena cava injuries, diaphragmatic perforation and spleen laceration. Retroperitoneal hematoma, incisional hernia, pancreatic fistula, hyponatremia and intestinal injuries are the most common postoperative complications. Intraoperative complications may be defined using the Satava classification that identify three grades: (I) an error without consequences; (II) an error with identification and immediate correction, which may lead to recovery; (III) an unrecognized error leading to a significant consequence or complication [29]. A postoperative complication is defined as an event that occurred within 30 days after surgery, and it can be defined using the Clavien classification modified by Dindo [Table 1] [30].

3. Discussion

In a few years, adrenalectomy has progressed from an operation with a large incision and prolonged hospitalization to a minimally invasive surgery with reduced postoperative pain, rapid mobilization, better cosmesis and shorter hospital stay. Since its introduction in 1992, the surgical indications for LTA have been widely increased [1,26,31]. Nowadays the technique is worldwide considered as the “gold standard” procedure for adrenal gland tumors <6 cm and is also considered safe and feasible for larger masses in selected cases [32–34]. On the other hands, PRA, popularized by Waltz, is considered a valid minimally invasive alternative procedure for adrenal tumors, demonstrated feasible for tumors <8 cm [20,35]. Despite an almost negligible mortality, postoperative morbidity rate after minimally invasive adrenalectomy are in a range from 3 to 20% [2,36]. Considering the need for a standardized classification system for surgical complications, in 1992 Clavien et al. published a paper describing a new approach for their categorization [30]. The scoring system was modified in 2004 by Dindo to include complications associated with increased risk of death and disability. However, this classification includes only postoperative complications that have a major impact on patient wellness. In 2005, Satava suggested a simple classification to evaluate surgical errors during minimally invasive surgery [29]. The aim of communicating intraoperative incidence includes the primary need to reduce their occurrence and it might contribute to a refinement of the strategy and surgical technique. Satava described that when a mistake is made there are three possible outcome: (I) an harmless error which can go unobserved, almost never reported; (II) an error with immediate identification and correction, with minimal or no consequences for the patient; (III) an error with consequence that the surgeon made and not recognize leading to a significant complication [29].

Considering the complications rate after LTA and PRA, is really important to evaluate several preoperative risk factors which could affect morbidity incidence [Table 2].

Many studies demonstrate that the size of the mass and the histopathological diagnosis of pheochromocytoma were independent risks factors of the perioperative complications rate [28,33,37]. Castillo et al. showed that LTA in large adrenal masses (>8 cm) is associated with prolonged operative time, increased blood loss and longer hospitalization, without affecting perioperative morbidity [38]. In fact in this series, 3 patients with pheochromocytoma >5 cm in diameter showed complications > Clavien III. Many Authors considered the tumor dimension >12 cm a contraindication to LTA [39,40]. Apparently in contrast with this conclusion, several recent studies indicated that LTA might be performed safely even for masses up to 15 cm [3–6,41–43]. LTA has been described as an effective and safe approach, even for pheochromocytoma >6 cm in diameter, although patients with such large tumors may have a higher conversion rate and more intraoperative hypertensive crises, representing in case of laparotomic conversion the first

Table 1
Clavien classification for postoperative complications modified by Dindo.

Grade	Definition
Grade I	Any deviation from a normal postoperative course without the need for pharmacological, surgical, endoscopic, or radiological intervention. Medical treatment is allowed such as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy.
Grade II	Requirement for pharmacological treatment with drugs other than those allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.
Grade III	Require surgical, endoscopic, or radiological intervention.
Grade IIIa	Interventions that not require general anesthesia.
Grade IIIb	Interventions under general anesthesia.
Grade IV	Complications that involve a vital risk for the patient and require management of intensive care (including complications of the central nervous system).
Grade IVa	Single organ dysfunction.
Grade IVb	Multi-organ dysfunction.
Grade V	Patient death.
'd'' suffix	In patients with a complication that will required follow-up after discharge complete assessment; the suffix “d” (disability) is added to the degree of complication.

Table 2
Predictive factors for postoperative complications after minimally invasive adrenalectomy.

Author	Number of patients	Predictive factors
LA Kulis, J Lap Adv Surg Tech 2012	306	Bilateral surrenectomies
PK Gupta, Surg Endosc 2011	988	Functional status, vascular periferic disease, ASA, comorbidites
A Valeri, Surg Endosc 2011	833	BMI, tumor size, age, PCC, experience
GAM Tiberio, Long Arch Surg 2012	163	Tumor size, metastases, PCC
JG Bittner IV, Surg Endosc 2013	402	Tumor size, associated procedures
S Hattori, J Endourol 2012	265	ASA
S Gaujoux, BJS 2011	462	Conversion, left surrenectomy
OA Castillo, Acta Urol Espanol 2014	322	PCC, comorbidities, obesity, previous surgery
HC Dancea, JSLS 2012	80	Obesity
S Permpongkosol, J Urol 2007	106	ASA
ZJ Shen, J Endourol 2007	456	Tumor size, BMI, PCC
A Hausch, Ann Surg Oncol 2014	7829	Experience, bilaterality, malignacy

PCC: Pheochromocytoma.
ASA: American Society of Anesthesiologists-physical status.

diagnostic step [11]. Several Authors proposed a laparoscopic approach also for pheochromocytoma of 6–8 cm only if great care is adopted to avoid capsular disruption and, if necessary, a prompt conversion to open surgery is cautiously considered to reduce patient risk [11,44]. Moreover, a relationship between pheochromocytoma size >6 cm, catecholamine concentrations, duration of anaesthesia and complications should be considered. The hyperkinetic, vasoconstrictive and hypovolemic hypertension caused by pheochromocytoma might be a main factor affecting the incidence of complications which can be reduced with a specific preoperative medical treatment [32,45]. The early ligation of adrenal vein may be considered a cornerstone for reducing the excessive catecholamine increase, and its delay has been advocated as responsible for the high complication rate in inexperienced hands [46].

Obesity is retained an important and spreading risk factors affecting morbidity after LTA. Erbil et al. showed a positive correlation between BMI and operating time, postoperative complications and hospitalization as the result of a suboptimal visualization in the context of increased amount of intraperitoneal fat [47]. Nevertheless, previous series did not led to the same conclusions, considering obesity only as increasing the conversion rate and the operative time [48–52]. Hattori et al. analyzed several possible risk factors for postoperative complication after minimally invasive adrenalectomy and concluded that the only independent risk factor is an ASA-PS (American Society of Anesthesiologists-physical status) > 3, a parameter related to the risk of anaesthesia and to the health state of the patient [48].

Gupta et al. showed a less incidence of post-surgical complications in centres with more than 30 adrenalectomies performed annually [53]. Also Bergamini et al. confirmed that the inexperience of a surgeon might be the most relevant risk factor in the occurrence of adverse events, especially in case of elevated BMI, large masses and pheochromocytoma [28]. One of the largest studies, published by Murphy et al., assay that in low flow surgical centers even if mortality remains low, major postoperative complications have significantly increased [54].

Still widely debated is the adequacy of laparoscopic surgery in case of malignant adrenal masses. As concluded by Agha et al., minimally invasive surgery of large adrenal tumors has to follow oncological principles such as sufficient resection margin, intact tumor capsule, no malignant cell dissemination and no risk for port site metastasis [33]. Miller at al. reported a worse oncological outcome in patient underwent LTA versus open surgery, with a shorter mean disease-free survival (9.6 months vs 19.2 months) and an higher recurrence rate (35% vs 28%), as confirmed also by several other studies [55–57]. Sommerey et al. advocate the choice of a traditional approach to achieve a complete resection of the tumor and a fine lymphadenectomy to reach a long-term cure [58]. Nevertheless, a recent German study including 152 patients showed a comparable frequency of tumor capsule laceration and peritoneal carcinomatosis between laparoscopy and open surgery, with the advantage in the minimally invasive group of an enhanced quality of life [59]. Furthermore a recent Italian paper underlined the importance of a multidisciplinary approach for adrenocortical cancer, reachable only in a dedicated high volume centre [60].

In the last years, there was a large diffusion of LTA and

Table 3
Comparative outcomes and complications of LTA versus PRA.

Author	Mean operative time (min)		Mean blood loss (ml)		Mean hospitalization (day)		Conversion (%)		Postoperative bleeding requiring surgery (%)		Mortality (%)	
	LTA	PRA	LTA	PRA	LTA	PRA	LTA	PRA	LTA	PRA	LTA	PRA
Naya et al. *2002*	202 ± 74	221 ± 87	113 ± 204	192 ± 365	9.0 ± 3.3	9.5 ± 3.5	4	3	0	0	0	0
Lombardi et al. *2008*	135 ± 47	114 ± 47	N.A.	N.A.	6.2 ± 2.4	5.6 ± 2.1	0	0	1	0	2[b]	0
Berber el 2009	157 ± 7	138 ± 6	35 ± 7	25±6[a]	N.A.	N.A.	2	2	0	0	0	0
Kiriakopoulos et al. *2011*	77.5	90.0	N.A.	N.A.	4	2[a]	0	0	0	0	0	0
Dickson et al. *2011*	144.8 ± 42.4	99.9 ± 23.3[a]	123.8 ± 204.3	8.4 ± 19.1[a]	3.1 ± 1.4	1.9 ± 0.9[a]	0	0	2	0	0	0
Lee et al. *2012*	108.3 ± 34.5	87.2 ± 27.6[a]	74.8 ± 145.2	20.0 ± 41.7	5.9 ± 3.6	3.0 ± 1.4[a]	0	0	0	0	0	0
Constantinidis et al. *2013*	131.7 ± 46.6	86.3 ± 49.5[a]	N.A	N.A.	3.5 ± 3.0	1.6 ± 0.9[a]	0	0	0	0	0	0
Cabalag et al. *2014*	105	90	N.A.	N.A.	2	1[a]	0	0	0	0	0	0

[a] Difference statistically significative.
[b] Death for cardiac and pulmonary complication.

subsequently of PRA as minimally invasive technique for adrenalectomy, however the best approach is still debated. Many studies have compared the outcomes of patients underwent LTA and PRA, showing similar results in terms of morbidity and mortality [61–63]. Anyway, as reported recently, thanks to the avoidance of pneumoperitoneum and the direct approach to the gland leading to minimal dissection of body wall or adjacent organs, PRA has several advantages such as shorter operative time, postoperative pain score at day one and three, significantly lower and shorter hospitalization with comparable morbidity rate [35,64] [Table 3]. Considering that PRA is performed only by surgeons with great LTA experience or those who undergo proper PRA training, that allow them to overcome the learning curve more easily, and moreover, due to the smaller extent of dissection required, median operative time is shorter for PRA than LTA [65–67]. In fact, one of the most important advantages of PRA is the direct approach to the adrenal gland and vein, avoiding the need to enter the peritoneal cavity or mobilize adjacent intra-abdominal organs, as well obviating adhesions from previous surgery, leading to a great saving of time. For this reason, PRA is feasible and ideal also for patients underwent a previous laparotomy [64]. In addition, in case of bilateral adrenalectomies, the prone position allows to approach both adrenal glands without the need to reposition the patient and sometimes two surgical staff might perform two operations at the same time [58,64]. Hospitalization of patients underwent PRA is generally shorter than the LTA patients (1 vs 2–3 days) as reported by many Authors [68–70]. It might be associated with the reduction of postoperative pain due to the avoidance of pneumoperitoneum, as suggested by the median visual analogue pain score value in patients undergoing PRA than LTA [68]. Another parameter indicating the postoperative pain is analgesic use, which is lower after PRA in many studies [62,64,66]. Kiriakopoulos et al. reported that the 60% of patient underwent PRA no required narcotic analgesia and were mobilized and started diet on the evening of surgery, demonstrating a faster recovery of bowel movements [68]. Analysing English literature, PRA and LTA were found to be similar in term of intra- and post-operative complications [15,35]. Constantinides et al. in a meta-analysis, reported an overall complications rate of respectively 9% and 6.4% for PRA and LTA. The incidence of haemo/pneumotorax was low in any techniques. There was no statistically significant difference for splenic injury and intra-abdominal abscess between the two approaches. Wound infection, chest infection or pleural effusion were also uncommon and similar in incidence. Conversion rate was from 2% to 14% in patients underwent PRA, while 1%–22% in LTA patients with no statistically significant difference [15,65,71–73]. Indications for conversion in PRA patients include failure to progress, inability to develop the retroperitoneal space or loss of pneumoretroperitoneum associated with surgeon inexperience [65,74]. A complication uniquely related to PRA was neuromuscular pain linked to subcostal nerve injury [19]. The main causes for conversion during LTA was bleeding, followed by intra-abdominal adhesions, failure to progress, splenic and pancreatic injury and inferior vena cava injury or infiltration [27,72,75]. Mortality rate is approaching 0% in both the techniques [15].

Despite several benefits, PRA might pose serious additional technical difficulties such as smaller working space, the requirement for the surgeon to learn a new “reverse angle” anatomic perspective and the uncomforting to work with tumors larger than 8 cm [33]. The need of a dedicated staff to know all the nuances of the patient position, equipment and anaesthesia in prone decubitus must to be considered an additional technical disadvantage. Moreover, as consequence of the high insufflation pressure of CO_2, tamponating the small vessel bleeding, the operating space seems “only apparently” dry.

4. Conclusion

Minimally invasive adrenalectomy is a safe and feasible procedure. PRA seems to be superior to LTA in terms of shorter operative time, hospitalization and postoperative pain with a comparable incidence of peri- and post-operative complications, especially in masses <8 cm. Nevertheless, many surgeons are still accustomed in performing the standardized LTA, which guarantee great outcomes, and change to a reverse angle anatomic approach would be a very hard challenge. Further studies are needed to compare these two techniques and to establish a definite superiority, excluding selection bias and bias due to surgeons experiences.

Conflicts of interest

All Authors have no conflict of interests.

Sources of funding

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Ethical approval

None.

Author contribution

GC: Partecipated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also partecipated substantially in the drafting and editing of the manuscript.

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