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REVIEW

Laparoendoscopic single site, laparoscopic or open surgery for adrenal tumors: Selecting the optimal approach

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Abstract

Numerous surgical modalities are available to treat adrenal lesions. Minimally-invasive approaches for adrenalectomy are indicated in most circumstances, and new evidence continues to be accumulated. In this context, current indications for open surgical adrenalectomy (OS-A), minimally-invasive adrenalectomy (MI-A), and laparoendoscopic single-site adrenalectomy (LESS-A) remain unclear. A comprehensive English-language literature review was performed using MEDLINE/PubMED to identify articles and guidelines pertinent to the surgical management of adrenal tumors. A comprehensive chart review was performed for three illustrative cases. Clinical recommendations were generated based on relevant literature and the expertise of the investigator group. MI-A offers advantages over OS-A in properly selected patients, who experience fewer complications, lower blood loss, and shorter hospital stays. Robot-assisted laparoscopic and retroperitoneoscopic adrenalectomy may offer advantages over transperitoneal surgery, and LESS-A may be an even less-invasive option that will require further evaluation. MI-A remains the surgical treatment of choice for most adrenal lesions. Tumor size and stage are the primary indications for selecting alternative treatment modalities. OS-A remains the gold standard for large tumors (> 10 cm) and suspected or known advanced stage malignancy. LESS-A appears to be an appropriate initial approach for small tumors (< 4-5 cm), including pheochromocytoma and isolated adrenal metastases.

Key words: Adrenal masses; Surgical approach; Indications; Open adrenalectomy; Laparoscopic adrenalectomy; Laparoendoscopic single-site adrenalectomy

Core tip: Minimally-invasive adrenalectomy remains the surgical treatment of choice for most adrenal lesions. Tumor size and stage are the primary indications for selecting alternative treatment modalities. Open surgical adrenalectomy remains the gold standard for large tumors (> 10 cm) and suspected or known advanced stage malignancy. laparoendoscopic single-site adrenalectomy appears to be an appropriate initial approach for small tumors (< 4-5 cm), including pheochromocytoma and isolated adrenal metastases.

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INTRODUCTION

Neoplasms of the adrenal gland consist of a broad spectrum of pathologies, ranging from benign non-functioning cortical adenomas (or "incidentalomas") to locally-invasive malignancies, such as adrenocortical carcinoma or metastasis from a distant site. Adrenalectomy

Table 1 Indications and relative contraindications for each surgical approach

Indications	Relative contraindications
OS-A	
Adrenocortical carcinoma with radiographic evidence of extra-adrenal extension (stage Ⅲ-Ⅳ)	Amenable to minimally-invasive approach
Extension of adrenal vein tumor thrombus into IVC	
Size larger than 10-12 cm	Size < 10 cm
Concomitant open procedure	
Paraganglioma	
Multiple prior abdominal surgeries	
MI-A	
Non-functioning and functioning adrenal tumors, including pheochromocytoma	Locally-advanced tumors (stage Ⅲ-Ⅳ)
Isolated adrenal metastases	Known, relatively large adrenocortical carcinoma (complete resection is essential for cure)
Size < 10 cm	Size larger than 10-12 cm
Adrenocortical carcinoma, consider only if stage Ⅰ-Ⅱ and < 10 cm	Multiple prior abdominal surgeries (or discussion of possibility of conversion)
BMI ⩾ 30 kg/m^2	
LESS-A	
For patients who consider cosmesis to be of great importance	Surgeon inexperience with LESS-A
Size < 4-5 cm	Size > 5 cm
Non-functioning and functioning adrenal tumors, including pheochromocytoma	Adrenocortical carcinoma
Isolated adrenal metastases	Multiple prior abdominal surgeries
BMI < 30 kg/m^2	

OS-A: Open surgical adrenalectomy; MI-A: Minimally-invasive adrenalectomy; LESS-A: Laparoendoscopic single-site adrenalectomy; BMI: Body mass index.

is the definitive therapy for these tumors and is indicated when either hormone secretion and/or increased risk for malignancy is present[1]. Risk factors for adrenal malignancy include evidence of a functional adrenal tumor, large tumor size, and concerning radiographic findings such as hyperdensity or heterogeneity, irregular tumor margins, local invasion, lymphadenopathy, or distant metastases[2-4].

Open surgical adrenalectomy (OS-A) using a dorsal lumbotomy, midline, subcostal, or thoracoabdominal incision is the historical gold standard, but has largely been replaced by minimally-invasive alternatives. Minimally-invasive adrenalectomy (MI-A) using a transperitoneal laparoscopic approach was first described in 1992[5] and has since replaced OS-A as the operation of choice for resecting most adrenal lesions[6]. Two notable exceptions to this include known adrenal malignancy and tumors that are excessively large or difficult to approach laparoscopically. MI-A is known to offer improved analgesia, hospital stay, blood loss, and complication rate compared to OS-A[7]. Several different techniques, including robot-assisted approaches, have been proposed to address various clinical scenarios where the traditional transperitoneal approach is technically difficult. Even more recently, laparoendoscopic single-site adrenalectomy (LESS-A) has emerged as an appropriate initial surgical approach for tumors smaller than 4-5 cm[8].

Some might suggest that the least invasive approach should be used in all circumstances, but our clinical experience would suggest that the optimal approach in a given scenario may depend on patient and tumor features, such as specific adrenal pathology, prior history of abdominal surgeries, tumor size, patient body habitus, and experience of the operating surgeon (Table 1)[9]. This report details a contemporary approach to surgical decision-making for adrenal tumors, with a review of the literature regarding OS-A, MI-A, and LESS-A.

LITERATURE REVIEW

A comprehensive English-language literature review was performed using MEDLINE/PubMed to identify articles and guidelines pertinent to the indications, techniques, perioperative results, and oncologic outcomes for various treatment modalities for adrenal tumors. Combinations of MeSH search terms adrenal tumor, pheochromocytoma, adrenal cortical carcinoma, metastasis, adrenalectomy, indications, laparoscopic, open, laparoendoscopic single site, transperitoneal, retroperitoneal, and robotic were used. A comprehensive chart review was conducted for the three patients in order to detail the factors determining the elected surgical approach. Approval was obtained from the institutional IRB. Clinical implications presented incorporate relevant literature and the expertise of the investigator group.

OS-A

Case 1: A 54-year-old female presented with worsening left lower abdominal pain that radiated to the left flank. Computed tomography with Ⅳ contrast revealed a large complex solid and cystic mass in the left retroperitoneal space measuring 13 cm and displacing the left kidney laterally and inferiorly. No retroperitoneal lymph nodes or visceral metastases were identified and subsequent chest X-ray was normal. She reported no history suspicious for a functional adrenal tumor, denying uncontrolled

Table 2 Outcomes from select studies comparing minimally-invasive adrenalectomy to open surgical adrenalectomy

Ref.	*N*	Mean tumor size (cm)	ACC or MET (%)[1]	OT (min)	EBL (mL)	LOS (d)	Conversion (%)	Complications (%)
Assalia *et al*[116]	581 MI-A	2.8	0.9	184	154	2.9	-	10.9
	753 OS-A	4.1	5.8	162	309	7.2	-	35.8
Lee *et al*[59]	358 MI-A	-	13.6	174	-	4.1	-	3.6
	311 OS-A	-	44.5	234	-	9.4	-	17.4
Eichhorn-Wharry *et al*[119]	1980 MI-A	-	4.1	146	-	2.8	-	1.8
	592 OS-A	-	18.4	186	-	6.7	-	7.6
Lombardi *et al*[120]	30 MI-A	7.7	100	135	-	5.3	0	3.4
	126 OS-A	9	100	129	-	9.3	-	5.6
Mir *et al*[121]	18 MI-A	7	100	298	1500	4	24	5.0
	26 OS-A	13	100	273	1100	6	-	20.0
Donatini *et al*[79]	13 MI-A	5.5	100	-	-	7	0	8.0
	21 OS-A	6.8	100	-	-	9	-	14.0
Bittner *et al*[122]	356 MI-A	3.2	5.9	159	-	2.5	6.2	11.0
	46 OS-A	8.5	28.2	197	-	9.1	-	50.0

[1]Preoperative indication of ACC or isolated adrenal metastasis. ACC: Adrenocortical carcinoma; MET: Metastasis to adrenal gland; OT: Operative time; EBL: Estimated blood loss; LOS: Length of hospital stay; OS-A: Open surgical adrenalectomy; MI-A: Minimally-invasive adrenalectomy.

blood pressure, new hair growth or other features of Cushing's syndrome. Functional work-up was pursued with serum potassium, urinary cortisol, and plasma and urinary metanephrines. After this negative functional evaluation was completed, the patient underwent OS-A *via* an anterior subcostal incision. The patient was discharged after an uneventful 5 d hospital stay and has remained without evidence of disease recurrence more than 3.5 year since surgery.

With expansion of the indications for MI-A, fewer OS-A are being performed worldwide. Nevertheless, there remain situations in which OS-A remains the best option, such as the case just described. Tumors larger than 10-12 cm should be resected *via* OS-A, given the increased likelihood of these lesions being malignant and the technical difficulties associated with laparoscopic removal of large tumors. OS-A remains the standard treatment for all patients with preoperative radiographic evidence of extra-adrenal tumor invasion. Tumors with associated adrenal and renal vein thrombus, which can extend into the inferior vena cava and right atrium, should also be resected *via* OS-A (Table 1). All these scenarios require maximal exposure to complete the procedure safely and extract the tumor intact. A summary of the evolution of indications for and outcomes of OS-A compared to MI-A are included in (Table 2).

MI-A

Case 2: The patient is a 54-year-old female who presents with a 7 cm × 5 cm × 4 cm right adrenal mass on follow up imaging obtained 12 mo after open right radical nephrectomy for pT2N0M0 clear cell renal cell carcinoma with negative lymph nodes. The patient has a relevant past medical history of renal cell carcinoma, rectal cancer s/p low anterior resection, and morbid obesity with a body mass index (BMI) of 61. Physical examination was unremarkable except for her large abdominal girth and prior incisions. Metastatic workup was negative for additional lesions. Biopsy of the adrenal mass was positive for metastatic renal cell carcinoma. After a discussion of risks and benefits of laparoscopic adrenalectomy and the possibility of open conversion, the patient underwent a transperitoneal laparoscopic adrenalectomy (TL-A). The procedure was successful, without any significant complications other than some delayed return of bowel function, and the patient was discharged home after a 5-d hospital stay.

Three aspects of this case indicate MI-A to be the appropriate surgical approach. MI-A is the procedure of choice for isolated adrenal metastases and for adrenal masses < 10 cm. MI-A is indicated for obese patients, as reduced morbidity and improved outcomes have been demonstrated when compared to OS-A[10]. An additional consideration in this case is the patient's past surgical history. This patient is likely to have adhesions, which may complicate laparoscopic surgery, but MI-A has been shown to be a feasible and safe initial approach to patients with previous abdominal surgery[11,12]. MI-A is an appropriate initial approach, with conversion to OS-A for failure-to-progress when adhesions make laparoscopic surgery excessively difficult.

Laparoscopic adrenalectomy: Transperitoneal vs retroperitoneal

TL-A is the most widely performed MI-A. TL-A offers a large working space, familiar anatomical exposure, excellent visibility, and the ability to perform simultaneous transperitoneal procedures[13]. This approach is dependent upon the ability to retract and mobilize the abdominal organs required for adequate exposure, and may require additional instruments to accomplish this prerequisite step. Adhesions from prior abdominal surgery can complicate port placement and lysis of adhesions may lengthen operative times and increase intra-operative risk of bowel injury, and should be considered carefully when deciding upon the surgical approach in any given scenario.

Retroperitoneal laparoscopic adrenalectomy (RL-A)

Table 3 Summary of the most recent meta-analyses comparing laparoscopic techniques for adrenalectomy

Ref.	RAL-A *vs* MI-A Brandao *et al*[30]	TL-A *vs* RL-A Nigri *et al*[27]	LESS-A *vs* MI-A Wang *et al*[41]
n	600	1205	443
Mean tumor size (cm)	3.86, 3.78	4.0, 3.3	2.7, 3.43
(Odds ratio, CI)	NA	0.48 (-0.21-1.18)	- 0.69 (-1.11--0.26)
P-value	NS	0.17	0.002
Mean operating time (min)	175, 148	132, 136	113.1, 92.7
(Estimate, CI)	5.88 (-6.02-17.79)	-11.07 (-41.38-19.24)	14.97 (4.69-25.24)
P-value	0.33	0.47	0.004
Mean EBL (mL)	44, 69	115, 85	74.2, 79.7
(Estimate, CI)	-18.21 (-29.11--7.32)	29.7 (-10.32-69.72)	-1.4 (-9.72-6.91)
P-value	< 0.0001	0.15	0.74
Mean LOS	3.78, 3.17	6.4, 5.5	3.82, 4.38
(Estimate, CI)	-0.43 (-0.56--0.30)	0.66 (-0.11-1.43)	-0.5(-1.02-0.02)
P-value	< 0.0001	0.09	0.06
Mean % conversion rate	4.4, 7.1	7.23, 7.74	7.8, 1.2
(Odds ratio, CI)	0.82 (0.39-1.75)	NA	4.66 (0.88-24.64)
P-value	0.61	NA	0.07
Mean % complication rate	3.6, 6.8	8, 6	14.2, 10.1
(Odds ratio, CI)	-0.04 (-0.07--0.00)	0.923 (0.58-1.46)	1.83 (0.88-3.81)
P-value	0.05	0.73	0.1

RAL-A: Robot-assisted laparoscopic adrenalectomy; MI-A: Minimally-invasive adrenalectomy; TL-A: Transpeitoneal laparoscopic adrenalectomy; RL-A: Retroperitoneal laparoscopic adrenalectomy; LESS-A: Laparoendoscopic single-site adrenalectomy; EBL: Estimated blood loss; LOS: Length of hospital stay.

allows for direct access to the adrenal gland without bowel mobilization or interference from intraperitoneal organs or adhesions. The disadvantages of RL-A, compared with TL-A, are the smaller operating space and relative absence of anatomic landmarks. This led some authors to conclude that RL-A should be reserved for surgeons with considerable experience with retroperitoneal surgery and tumors smaller than 5-7 cm[13,14]. Recent studies have demonstrated the safety and feasibility of treating tumors up to and exceeding 10 cm[15,16]. BMI > 35 kg/m^2 has also been cited as a contraindication to RL-A because of the difficulty in establishing and maintaining this potential space, resulting in limited exposure[14,15,17].

Numerous studies have been published comparing these two approaches[13,17-24]. These generally favor the retroperitoneal approach. Meta-analyses of these studies have demonstrated that operative time, blood loss, duration of hospitalization, time to oral intake, overall and major morbidity, and mortality are equivalent or superior for RL-A compared to TL-A[25-27]. A summary of the meta-analysis performed by Nigri *et al*[27] is included in (Table 3). RL-A may be preferred to TL-A for a few select scenarios, such as patients with suspected adhesions from previous transperitoneal abdominal surgery. However, it should be noted that the retroperitoneal space is typically obliterated after nephrectomy, preventing insufflation of this space independent of the peritoneal cavity. Some surgeons use the prone position for RL-A, allowing bilateral procedures to be performed without repositioning the patient. For bilateral RL-A (or TL-A) in full or modified lateral decubitus position, repositioning is a necessity in all but the thinnest of patients. With RL-A, some have reported success with two surgical teams operating simultaneously to reduce operative time and surgical stress[28,29].

Robot-assisted laparoscopic adrenalectomy

Robot-assisted laparoscopic adrenalectomy (RAL-A) offers improved blood loss and hospital stay, and similar operative time, conversion rate, and postoperative complications when compared to traditional MI-A[30]. A summary of Brandao *et al*[30] meta-analysis comparing RAL-A to MI-A is included in (Table 3). This procedure may offer advantages in morbidly obese patients (> 30-35 kg/m^3) and those with larger tumors, by improving retraction and exposure[31-34]. The main disadvantages cited by most authors are the learning curve of the entire surgical team, particularly for those not regularly performing other robotic surgeries, and the potential added cost of robot-assisted surgery. Overall, this approach shows promise to enable a wider range of tumors to be addressed with MI-A, and is likely to become more commonly utilized in the future.

LESS-A

Case 3: The patient is a 72-year-old male presenting with an incidentally-detected adrenal mass found during staging evaluation of a suspicious lung lesion. The patient was not found to have signs or symptoms of a functioning adrenal tumor upon investigation. Relevant past medical history includes hypertension, coronary artery disease and hyperlipidemia, with no prior surgical history. The patient has a 58 pack-year smoking history and physical examination was unremarkable. The patient was referred to a multi-disciplinary clinic for evaluation of a

Table 4 Laparoendoscopic single-site adrenalectomy *vs* minimally-invasive adrenalectomy: Overview of the outcomes from available comparative studies (adapted from Rane *et al*[8] and Wang *et al*[41])

Ref.	*N*	Mean tumor size (cm)	ACC or MET (%)[1]	OT (min)	EBL (mL)	LOS (d)	Conversion (%)	Complications (%)
Jeong *et al*[36]	9 TLESS-A	2.9	0	169	178	3.2	11 (1 to MI-A)	11
	17 MI-A	4.3	0	145	205	3.5	5.8 (1 to OS-A)	5.8
Walz *et al*[40]	47 RLESS-A	2.3	2.1	56	< 10	2.4	8.5 (to TLESS-A)	8.5
	47 TLESS-A	2.6	0	40	< 10	3.1	0	6.4
Ishida *et al*[39]	10 TLESS-A	2.8	0	125	12	5.2	0	0
	10 MI-A	4.5	0	120	15	6.9	0	0
Shi *et al*[38]	19 RLESS-A	2.1	0	55	30	6	0	11
	38 MI-A	2.4	0	42	18	6	0	7.9
Kwak *et al*[123]	10 TLESS-A	3.3	0	127	-	4.5	0	10
	12 MI-A	3	8	113	-	4.1	0	-
Vidal *et al*[124]	20 TLESS-A	3	0	95	Min	3.0	0	0
	20 TL-A	3	0	80	Min	2.5	0	0
Wang *et al*[125]	13 TLESS-A	2	7.7	149	79	5.2	0	31
	26 TL-A	2.4	0	113	93	6.3	0	12
Tunca *et al*[126]	22 TLESS-A	3.3	0	64	48	2.45	-	0
	74 TL-A	4.7	4.1	68	38	3	-	0
Lin *et al*[127]	21 RLESS-A	-	0	145	Min	2	0	0
	28 MI-A	-	0	95	50	4	0	3.6

[1]Preoperative indication of ACC or isolated adrenal metastasis. ACC: Adrenocortical carcinoma; MET: Metastasis to adrenal gland; OT: Operative time; EBL: Estimated blood loss; LOS: Length of hospital stay; TLESS-A: Transperitoneal LESS-A; RLESS-A: Retroperitoneal LESS-A.

2.5 cm, spiculated right upper lobe lung mass. A recommendation was made for biopsy of the lung lesion and this revealed moderately differentiated adenocarcinoma. A staging evaluation with PET/CT imaging revealed only a single lesion suspicious for metastatic disease: a 1.2 cm, solid left adrenal mass. Initial recommendation was for percutaneous biopsy by interventional radiology, but based on the small size and location of the lesion adjacent to the aorta, the patient was advised that surgical excision of the lesion was the recommended course. After discussion of risks and benefits with the patient, including the possibility of conversion to multi-port TL-A or OS-A, the patient was scheduled for transperitoneal LESS-A. The patient was discharged home after an uneventful 1 d hospital course. He subsequently underwent thoracotomy and wedge excision of the lung mass and remained without significant disease progression until brain metastasis was detected 2.5 year later.

The first case of LESS-A was reported in 2008[35]. Since then, several studies have compared this emerging technique with MI-A, demonstrating reduced postoperative pain, shorter hospital stay, improved cosmesis, comparable blood loss and complication rate, but with longer operative times[36-40]. A summary of all studies comparing LESS-A to MI-A is included in (Table 4). Rane *et al*[8] published a meta-analysis for LESS-A in 2012. Cumulatively, they found that LESS-A was performed for 59 functioning adenomas (Cushing's syndrome or Conn's Syndrome), 28 pheochromocytomas, and 15 non-functioning masses (adenoma, adrenal metastasis, others). They proposed early and advanced indications for LESS-A based on surgeon experience. Accepted indications for surgeons early in their operative experience include adrenal tumors up to 4 cm in size, functioning or non-functioning, that are localized, and suspected to be benign, in non-obese patients without previous abdominal surgery. Indications for surgeons with advanced LESS experience might include any adrenal neoplasm up to 10 cm in size, with consideration of moderately obese patients and those with limited prior abdominal surgery. Wang *et al*[41] published an updated meta-analysis comparing LESS-A to MI-A in 2013. A summary of this article's findings is included in (Table 4).

Unfortunately, the data on this procedure is limited at present and long-term oncologic outcomes are not yet available. Four of the nine studies included by Wang *et al*[41] had less than 15 patients. Though a learning curve for LESS-A has not been formally demonstrated, extrapolation from other LESS procedures suggests that this is likely within the surgeon's learning curve. Additionally, the patients in these studies have been carefully selected, as demonstrated by the smaller tumor size compared to MI-A. These limitations notwithstanding, LESS-A appears to be an appropriate initial approach when cosmesis is of the utmost importance in the setting of small (< 4-5 cm) adrenal tumors or metastases, that can readily be converted to MI-A with the placement of one or more accessory ports to aid with retraction and exposure. These indications are subject to change as new literature arises, better informing the optimal utilization of this emerging technology.

DISCUSSION

Pathology-benign

MI-A is the surgical approach of choice for almost all benign adrenal tumors. Functional adrenalomas, including aldosteronomas, pheochromocytomas, and cortisol-secreting adenomas, have been demonstrated to be amenable to MI-A[42-49]. For pheochromocytomas,

recurrence rates following MI-A are low (6%-8%) and not significantly different from OS-A in reports that are somewhat limited by short follow-up durations (21-102 mo)[50-54]. Most experts believe that size and tumor biology, rather than surgical approach, are more likely to determine the chance of cure in this disease[55,56]. Based on this literature, many authors and guideline-producing societies have concluded that MI-A is an appropriate initial approach to pheochromocytomas[50-57]. Recurrence of other benign adrenal tumors is extremely rare and is generally limited to tumors that are later discovered to be malignant based on metastasis after initially benign or indeterminate pathology. Advantages of this procedure compared to OS-A are well documented and include lower or equivalent blood loss, improved postoperative pain control, shorter hospitalization, improved perioperative convalescence, and excellent cosmesis[7,58-60]. Results concerning operative time for MI-A compared to OS-A have been mixed, with some series reporting longer times for MI-A[61,62], others reporting comparable durations[63,64], and still others shorter times[59,65]. Operative mortality is very low for adrenalectomy, and has not been shown to be significantly different between the two procedures[60]. At this time, selecting amongst different MI-A approaches should be determined by surgeon familiarity and experience, as there is inadequate evidence to demonstrate superiority of any one MI-A approach for a specific benign adrenal pathology.

Pathology-malignant

Adrenocortical carcinoma (ACC) is a rare disease with an annual incidence of approximately 1 per million population[66]. Overall 5 years survival is approximately 38% to 46%[66,67]. Unfortunately, only 30% of cases are detected prior to extension outside the adrenal gland or metastasis[67]. Cure of ACC is dependent upon complete surgical resection, including regional lymph nodes and involved adjacent organs[68-71]. OS-A has been the gold standard for ACC for decades[3,4]. This status has been challenged in recent years, by reports of favorable perioperative and oncologic outcomes with MI-A for ACC[72-79]. However, the use of MI-A for known ACC remains controversial, in large part based on the poor outcomes reported during initial experiences with MI-A, which included intraoperative tumor fragmentation, port-site and local recurrences, and peritoneal carcinomatosis[80-83]. Two recent studies reported that MI-A was associated with increased frequency of positive margins and intraoperative tumor spillage, shorter time to recurrence, and worse overall survival for stage Ⅱ ACC compared to OA[84,85]. These authors concluded that MI-A is inappropriate in known or suspected ACC. In contrast, numerous recent reports have described improved perioperative and equivalent or even superior oncologic outcomes for MI-A performed with contemporary techniques[74,77-79,86]. These advocates argue that so long as standard oncologic principles are strictly adhered to, comparable outcomes can be achieved for stage Ⅰ and Ⅱ ACC tumors by those with the requisite experience and expertise. Current guidelines remain equivocal, with some suggesting that MI-A is acceptable as an initial surgical approach for stage Ⅰ and Ⅱ ACC < 10 cm and others recommending OS-A for all suspected or known ACC. All guidelines currently recommend conversion to OS-A when extensive tumor adhesion, invasion, or lymphadenopathy is identified intraoperatively[50,87-89].

Pathology-metastasis

Metastasis to the adrenal gland is commonly seen in cancer of the breast, lung, colon, melanoma and lymphoma. Adrenal metastasectomy has been shown to improve survival in patients with limited metastatic burden, with average survival rates of between 20 and 30 mo after surgery compared with 6 to 8 mo without resection. Nevertheless, this heterogeneous population of patients has approximately 25% 5 year survival[3,90]. Despite poor durable oncologic outcomes post-adrenalectomy, there is also a role for this procedure as a palliative measure[91]. For the treatment of isolated adrenal metastatic disease, MI-A was initially controversial, but has since become the standard approach. Published series have demonstrated that this is a safe procedure with very low morbidity and similar long-term outcomes to OS-A[90,92-95]. In the largest and most compelling comparison of MI-A and OS-A for adrenal metastases, Strong *et al*[94] reviewed 94 adrenalectomies (31 MI-A *vs* 63 OS-A) and found no differences in margin status, local recurrence, disease-free survival, or overall survival. They also demonstrated that MI-A provided significantly shorter operative time, lower estimated blood loss, shorter length of hospital stay, and fewer total complications. These authors concluded that MI-A should be recommended as an appropriate initial approach to isolated adrenal metastases. Several additional studies comparing MI-A to OS-A for adrenal metastases reported similar results[91,93,96]. In accordance with these findings, guidelines have recommended that MI-A is appropriate for solitary metastases to the adrenal gland, given that local invasion is not present[50,87].

Prior abdominal surgery

Previous abdominal surgery is a known risk factor for laparoscopic procedures[97]. Some authors have considered this to be a relative contraindication to transperitoneal MI-A and recommend a retroperitoneoscopic approach[14,98-100]. Morris *et al*[11] analyzed 92 patients with and 154 patients without previous abdominal surgeries undergoing TL-A. Operating time, blood loss, and perioperative complications were not significantly different between the two groups. They concluded that TL-A was safe in patients with previous abdominal surgeries, conversion to OS-A occurs infrequently, and is rarely attributed to adhesions, and that surgeons should perform the surgical method they are most comfortable with. The laparoscopic approach can be tailored to accommodate patients with previous transabdominal surgery

with modification of port placement or addition of accessory ports, and should not be contraindicated in these patients. Maintaining a low threshold for conversion to OS-A for failure-to-progress can maintain an equivalent level of safety with MI-A to that obtained with an initial plan for OS-A.

Tumor size

Historically, tumor size > 5 cm was considered to be a relative contraindication to MI-A given the increased risk of treating incidentally-found ACC, along with greater complexity of procedure, longer operative time and increased blood loss[101-104]. In recent years, numerous studies have demonstrated that MI-A is safe and feasible for large (> 5 cm) adrenal masses, offering favorable outcomes, reduced convalescence, and decreased morbidity compared to OS-A[105-112]. Boylu *et al*[111] compared MI-A for adrenal tumors < 8 cm and ≥ 8 cm. They found that operative time and blood loss were significantly higher for tumors ≥ 8 cm, but noted that results were comparable between the two groups concerning transfusion rates, length of hospital stay, and conversion to open surgery. They concluded that MI-A achieved favorable morbidity and surgical outcomes for larger lesions, despite being technically difficult operations. Other studies have demonstrated mixed results regarding the impact larger tumor size has on operative time, blood loss, hospital stay, and conversion to OS-A[110,113-115]. Hemal *et al*[109] recommended TL-A over RL-A for larger masses, given the larger working space it provides, and concluded that size alone should not eliminate MI-A as an option. Assalia and Gagner[116] performed a meta-analysis of 20 case-control studies examining MI-A versus OS-A. They noted that a few studies reported MI-A for lesions up to 14-15 cm, but found that most authors cited 10-12 cm as the maximum acceptable for MI-A. Overall, we feel that MI-A is appropriate for adrenal tumors up to 10-12 cm, in the absence of pre-operative imaging suggesting peri-adrenal infiltration or venous invasion or biopsy-proven ACC.

Body habitus

The body habitus of the patient, including both BMI and abdominal girth, must be accounted for when determining the approach for adrenalectomy. Laparoscopic procedures may be preferable in obese patients. Fazeli-Martin *et al*[10] compared open and laparoscopic approaches for adrenal and renal procedures in obese patients, demonstrating that patients undergoing laparoscopic procedures had decreased blood loss, less narcotic use, shorter hospital stay, and fewer complications, compared to open procedures. It is however, important to note that obesity has been independently associated with increased operative time and postoperative complications compared to non-obese patients for MI-A[117,118]. Two studies have been published comparing different MI-A approaches in this patient subgroup. Epelboym *et al*[23] analyzed 81 RL-A and 130 TL-A procedures in obese patients. They found that operative time (90 min *vs* 130 min; $P < 0.001$) and estimated blood loss (0 mL *vs* 50 mL; $P < 0.001$) were significantly less for RL-A, but failed to demonstrate significant differences for length of stay, overall mortality, incidence and severity of postoperative complications, and rates of readmission. Aksoy *et al*[32] compared 42 retroperitoneal RAL-A and 57 RL-A procedures in obese patients. They found no difference in perioperative outcomes between these two approaches. Given the paucity of data comparing MI-A approaches in obese patients, we cannot provide specific recommendations at this time as to which approach is best. Patient body habitus should be included in patient selection and determination of operative approach, as MI-A may be beneficial in these patients despite the increased procedural difficulty and associated morbidity.

CONCLUSION

While the indications for adrenalectomy have remained reasonably stable over the last two decades, the surgical approaches have become less and less invasive. Despite these technological advances, the least-invasive procedure (LESS-A) is not always the most appropriate. Various approaches to MI-A remain the preferred surgery for many situations, with LESS-A appearing to be a viable alternative for small tumors in relatively uncomplicated scenarios, though further validation is needed for this emerging technique. There remains a clearly defined role for OS-A for large and locally-advanced malignancies. Most importantly, the surgeon should engage each patient in the medical-decision making process for each adrenal tumor encountered.

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