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GUIDELINES

SAGES guidelines for minimally invasive treatment of adrenal pathology

Dimitrios Stefanidis · Melanie Goldfarb · Kent W. Kercher · William W. Hope · William Richardson · Robert D. Fanelli

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Preamble

The guidelines for Minimally Invasive Surgical Treatment of Adrenal Pathology are a series of systematically developed statements to educate and guide the surgeon (and patient) in the appropriate use of minimally invasive techniques for the treatment of adrenal disease. The guidelines address the indications, risks, benefits, outcomes, alternatives, and controversies of the procedures used in specific clinical circumstances. The statements included in these guidelines were derived from a systematic review of published work on the topic, and the recommendations are explicitly linked to the supporting evidence. The strengths and weaknesses of the available evidence are highlighted, and expert opinion is sought where published evidence lacks depth.

D. Stefanidis (✉)
Division of Gastrointestinal and Minimally Invasive Surgery, Department of General Surgery, CMC Surgical Specialty Center, Suite 300, 1025 Morehead Medical Plaza, Charlotte, NC 28204, USA
e-mail: dimitrios.stefanidis@carolinashealthcare.org

D. Stefanidis · K. W. Kercher
Carolinas HealthCare System, Charlotte, NC, USA

M. Goldfarb
Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

W. W. Hope
South East Area Health Education Center, Wilmington, NC, USA

W. Richardson
Ochsner Clinic Foundation, New Orleans, LA, USA

R. D. Fanelli
The Guthrie Clinic, Ltd, Sayre, PA, USA

Disclaimer

Clinical practice guidelines are intended to indicate the best available approach to medical conditions as established by a systematic review of available data and expert opinion. The approach suggested might not be the only acceptable approach given the complexity of the health care environment. These guidelines are intended to be flexible because the surgeon must choose the approach best suited to the individual patient and the variables in existence at the moment of decision. These guidelines are applicable to all physicians appropriately credentialed and address the clinical situation in question, regardless of specialty.

The guidelines were developed under the auspices of the Society of Gastrointestinal and Endoscopic Surgeons (SAGES) by the guidelines Committee and are approved by the Board of Governors. The recommendations of each guideline have undergone multidisciplinary review and were considered valid at the time of production based on the data available. New developments in medical research and practice pertinent to each guideline are reviewed, and the guidelines will be updated periodically.

Literature review method

A systematic literature search was performed on MEDLINE in April 2011. The search strategy was limited to adult English language articles, as shown in Fig. 1.

Fig. 1 Literature search strategy

Search: Laparoscopic Adrenalectomy--Robotic and Open Adrenalectomy & Related Diseases.

April 18, 2011

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1948 to Present>

Search Strategy:

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1 exp Adrenal Gland Diseases/ (51588)

2 exp Laparoscopy/ (55811)

3 exp **Robotic**s/ (8395)

4 1 and 2 and 3 (16)

5 from 4 keep 1-14 (14)

6 exp Neoplasm Metastasis/ (133900)

7 exp **Carcinoma/** (417996)

8 exp Adrenal Gland Neoplasms/ (21285)

9 exp **Pheochromocytoma/** (12738)

10 exp **Hyperaldosteronism/** (6777)

11 exp Adenoma/ (75036)

12 1 and 2 and 6 (18)

13 1 and 3 and 6 (0)

14 1 and 2 and 7 (75)

15 1 and 3 and 7 (1)

16 2 and 9 (393)

17 3 and 9 (11)

18 2 and 10 (144)

19 3 and 10 (2)

20 2 and 11 (629)

21 3 and 11 (23)

Fig. 1 continued

22 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 (1110)

23 limit 22 to (english language and humans and yr="1995 -Current" and "all adult (19 plus years)" and humans and comparative study) (104)

24 exp **Adrenalectomy/** (16616)

25 23 and 24 (66)

26 5 or 25 (79)

27 from 5 keep 1-4,6-14 (13)

28 open adrenalectomy.mp. (191)

29 22 and 28 (71)

30 limit 29 to (english language and yr="1995 -Current" and "all adult (19 plus years)" and comparative study) (28)

31 25 or 27 or 30 (79)

The literature search identified 79 relevant articles. The abstracts were reviewed by four committee members (D. S., W. W. H., M. G., and K. W. K.) and divided into the following categories:

(a) Randomized studies, metaanalyses, and systematic reviews
(b) Prospective studies
(c) Retrospective studies
(d) Case reports
(e) Review articles.

Randomized controlled trials, metaanalyses, and systematic reviews were selected for further review together with prospective and retrospective studies when a higher level of evidence was lacking. For inclusion, prospective and retrospective studies had to report outcomes for at least 50 adrenalectomies. Studies with smaller samples were considered when additional evidence was lacking. The most recent reviews also were included. All case reports, old reviews, and smaller studies were excluded. Duplicate publications or patient populations were considered only once. Whenever the available evidence from level 1 studies was considered to be adequate, lower-evidence-level studies were not considered. Newer relevant articles published after the original literature search date during the drafting of these guidelines also were included. According to the exclusion criteria, 70 articles were selected for review.

The reviewers graded the level of evidence and searched the bibliography of each article for additional articles that may have been missed during the original search. Additional relevant articles ($n = 94$) were obtained and included in the review for grading. A total of 164 graded articles relevant to this guideline were included in this review. To facilitate the review by multiple reviewers, these articles were divided into the following topics and distributed to the reviewers:

- Minimally invasive adrenalectomy outcomes and comparison with open technique
- Description and comparison of various minimally invasive surgery (MIS) adrenalectomy techniques
- Management of large adrenal tumors
- Management of adrenal cortical carcinoma and metastatic disease
- Management of pheochromocytoma
- Other circumstances (e.g. partial and bilateral adrenalectomy).

The recommendations included in these guidelines were devised based on the reviewers' grading of all the articles. It also should be noted that references to the size of the adrenal gland in this document reflect findings in imaging studies.

Levels of evidence

The quality of the evidence and the strength of the recommendation for each of the guidelines were assessed according to the GRADE system. This system has four-tiered scoring for quality of evidence [very low (⊕), low (⊕⊕), moderate (⊕⊕⊕), or high (⊕⊕⊕⊕)] and two-tiered scoring for the strength of the recommendation (weak or strong) [1, 2].

Introduction

Adrenal tumors have been found in 8.7 % of autopsy series, with adrenal incidentalomas reported in 4–7 % of patients undergoing abdominal imaging studies. Adrenal pathology that requires surgical resection spans a large spectrum of diseases. A description of the presenting symptoms of adrenal disease and their diagnostic workup is beyond the scope of these guidelines. Readers are referred to the existing comprehensive joint guideline by the American Association of Clinical Endocrinologists and the American Association of Endocrine surgeons (http://endocrinesurgery.org/documents/pguidelines/AdrenalGuidelines.pdf). This guideline focuses on minimally invasive surgical outcomes for adrenal disease and a comparison of different surgical approaches. The focus of the current guideline begins after the decision to perform an adrenalectomy has been made.

Outcomes of minimally invasive adrenalectomy

Since the first description of a laparoscopic adrenalectomy (LA) by Michel Gagner in 1992, LA has quickly become the standard of care for removing the majority of adrenal masses [1, 2]. Multiple prospective and retrospective studies have demonstrated minimal morbidity, short convalescence, and excellent cosmesis with LA [1, 3–30]. These results apply to functional and nonfunctional tumors.

Recently, similar outcomes have been published for the pediatric and nonadrenal cancer patient populations [31–37]. Most patients spend 1 or 2 nights in the hospital, with a few centers performing outpatient adrenalectomies for appropriately selected patients [15, 38, 39]. However, as with many technologically advanced procedures, high-volume surgeons continue to have the best outcomes [40].

Comparison with open adrenalectomy

Studies comparing open and laparoscopic adrenalectomies have demonstrated in the laparoscopic group improved postoperative pain levels [41–56], decreased morbidity [26, 41, 46, 57, 58], lower [11, 42, 44, 45, 48, 49, 52, 53, 59–63] or equivalent [47, 50, 54, 55, 57, 64, 65] operative blood loss, shorter hospital stays [11, 26, 41–48, 50, 51, 57, 59, 64, 66], and quicker return of bowel function and faster recovery. No significant differences in mortality have been demonstrated for a procedure that generally is associated with very low mortality.

Whether the open or laparoscopic approach leads to shorter operating time is less clear. Some series report longer operating times with the laparoscopic approach [41, 42, 45, 46, 48–52, 59, 64, 65], whereas others report similar durations of surgery [11, 17, 43, 44, 47, 53–55, 57, 60, 62, 63, 66, 67], and still others report shorter surgery durations [26, 61] than with the open approach (Table 1).

Specifically for pheochromocytomas, which generally are more technically demanding resections due to the inflammatory process and increased vascularity surrounding the adrenal gland, comparative studies have reported a lower estimated blood loss and a shorter postoperative stay for the laparoscopic approach [53, 54, 56, 60–63, 65, 67]. Operative duration, morbidity, and mortality were found to be similar in the majority of published studies [53–55, 60–63, 67]. Furthermore, most studies have reported similar effects of the two surgical approaches on intraoperative patient hemodynamics [53, 55, 56, 60, 62, 65, 67], whereas some have reported fewer episodes of intraoperative hypertension [54, 61] or hypotension [63] when the laparoscopic approach was used (Table 2).

Two retrospective studies comparing laparoscopic and open adrenalectomies performed for patients with hyperaldosteronism reported significantly decreased morbidity [57, 58] and shorter hospital stays [57] in the laparoscopic group.

Recommendation

Minimally invasive adrenalectomy is associated with less postoperative pain, a shorter hospital stay, earlier recovery, and similar long-term outcomes compared with open surgery and has been established as the preferred approach for all nonprimary adrenal cancer pathologies (+++, strong).

Adrenalectomy techniques

Several different techniques have been proposed and currently are used for the resection of adrenal tumors. A description of each approach as well as its advantages and disadvantages presented in the following sections (Tables 3, 4, 5, 6).

Lateral transabdominal adrenalectomy

Lateral transabdominal adrenalectomy (LTA) is the most common adrenalectomy technique used by general surgeons [68]. Compared with the retroperitoneal approach, LTA provides greater working space, which can be beneficial for very large tumors and morbidly obese patients, in which the use of extra-long bariatric instruments facilitates the procedure [1, 2, 6–8, 24, 69–72] (Table 3). In addition,

Table 1 Comparative studies of laparoscopic versus open adrenalectomy

Author (year)	No. of patients	Laparoscopic technique	EBL ml (*p* value)	Hospital stay days (*p* value)	OR time min (*p* VALUE)	Tumor size cm (*p* value)	Morbidity % (*p* value)	Mortality % (*p* value)
Lang et al. [61]	108	Retroperitoneal	74 vs 187 (<0.001)[a]	5.2 vs 8.3 (<0.001)[a]	52 vs 120 (<0.001)[a]	4.5 vs 4.9 (<0.05)	3.6 vs 12 (NS)	0 vs 0 (NS)
Thompson et al. [41]	100	Lateral transabominal	NR	3.1 vs 5.7 (NS)[a]	167 vs 127 (NS)[b]	2.9 vs 2.9 (NS)	0 vs 54 (NS)[a]	0 vs 0 (NS)
Brunt et al. [42]	66	Lateral transabdominal	104 vs 408 (<0.001)[a]	3.2 vs 8.7 (<0.01)[a]	183 vs 132 (<0.001)[b]	2.7 vs 3.4 (NS)	NR	NR
Lee et al. [26]	669	NR	NR	4.1 vs 9.4 (<0.001)[a]	174 vs 234 (<0.001)[a]	NR	3.6 vs 17.4 (<0.001)[a]	0.8 vs 1.6 (NS)
Barreca et al. [43]	172	Lateral transabodminal	208 vs 269 (NS)	4.2 vs 10 (<0.001)[a]	132 vs 168 (NS)	3.8 vs 3.9 (NS)	5.0 vs 9.6 (NS)	1.2 vs 1.0 (NS)
Kwan et al. [11]	486	Lateral/anterior transabdominal	50 vs 300 (<0.01)[a]	6.8 vs 12.4 (<0.01)[a]	154 vs 213 (NS)	5.4 vs 6.7 (<0.01)[b]		0 vs 0.6 (NS)
Chotirosnramit et al. [59]	80	Lateral transabdominal	50 vs 150 (<0.001)[a]	6 vs 10 (<0.001)[a]	135 vs 75 (<0.001)[b]	5.1 vs 5.7 (0.223)	4.8 vs 5.1 (NS)	0 vs 0 (NS)
Wu et al. [44]	67	Lateral transabdominal	104.04 vs 355.00 (0.021)[a]	3.9 vs 8.4 (<0.001)[a]	192.89 vs 203.43 (0.776)	3.3 vs 4.2 (0.318)	5.4 vs 3.3 (0.634)	0 vs 2.2 (NS)
Hallfeldt et al. [45]	70	Lateral transabdominal	260 vs 380 (<0.05)[a]	7 vs 10 (<0.05)[a]	135 vs 106 (<0.05)[b]	3.8 vs 3.7 (NS)	2.5 vs 3.3 (NS)	0 vs 0 (NS)
Tanaka et al. [47]	54	Lateral transabdominal/posterior retroperitoneal	200 vs 400 (NS)	8 vs 15 (0.005)[a]	240 vs 288 (NS)	3.5 vs 4.1 (NS)	20 vs 14 (NS)	0 vs 0 (NS)
Imai et al. [48]	80	Lateral transabdominal	40 vs 162 (<0.001)[a]	12 vs 18 (<0.001)[a]	180 vs 127 (<0.001)[b]	2.8 vs 2.7 (NS)	5 vs 2.5 (NS)	0 vs 0 (NS)
Shen et al. [58]	80	Lateral transabdominal/posterior retroperitoneal	NR	NR	NR	NR	0 vs 12.5 (<0.05)[a]	NR

The first value in each box reflects laparoscopic outcomes and the second open surgery outcomes

EBL estimated blood loss, *OR* operating room, *NS* not significant, *NR* not recorded

[a] Statistically significant, favoring laparoscopic procedure

[b] Statistically significant, favoring open procedure

Table 2 Comparative studies of laparoscopic versus open adrenalectomy for pheochromocytoma

Author (year)	No.of patients	Laparoscopic technique	EBL ml (*p* value)	Hosp ital stay days (*p* value)	OR time min (*p* value)	Tumor size cm (*p* value)	Intraoperative hypotension/ hypertension % (*p* value)	Morbidity % (*p* value)	Mortality % (*p* value)
Tiberio et al. [60]	22	Lateral transabdominal	48 vs 164 (<0.05)[a]	5 vs 8 (<0.05)[a]	158 vs 180 (NS)	4 vs 4.1 (NS)	33 vs 46 (NS)	0 vs 0 (NS)	0 vs 0 (NS)
Humphrey et. al [67]	44	Lateral transabdominal	NR	3 vs 6 (<0.05)[a]	138 vs 122 (0.94)	3.9 vs 5 (0.01)[b]	43 vs 29 (NS)	NR	NR
Lang et al. [61]	106	Retroperitoneal	74 vs 187 (<0.001)[a]	5.2 vs 8.3 (<0.001)[a]	52 vs 120 (<0.001)[a]	4.5 vs 4.9 (<0.05)	9 vs 18 episodes (<0.05)[a]	3.6 vs 12 (NS)	0 vs 0 (NS)
Hemal et al. [53]	16	Retroperitoneal	140 vs 592 (<0.05)[a]	4.4 vs 9.8 (<0.05)[a]	141 vs 169 (NS)	4.16 vs 4.8 (NS)	0 vs 0 (NS)	20 vs 57 (NS)	0 vs 0 (NS)
Davies et al. [65]	24	NR	NR	5 vs 11 (<0.01)[a]	236 vs 147 (<0.01)[b]	NR	NR	NR	0 vs 0 (NS)
Ichikawa et al. [62]	21	Lateral transabdominal/ retroperitoneal	55 vs 330 (0.01)[a]	12 vs 14 (NS)	145 vs 165 (NS)	3.6 vs 4.1 (NS)	NR	0 vs 0 (NS)	0 vs 0 (NS)
Edwin et al. [54]	16	Lateral transabdominal	200 vs 300 (NS)	3 vs 6 (0.001)[a]	110 vs 125 (NS)	6 vs 6 (NS)	1 vs 2 episodes (0.008)[a]	0 vs 33 (NS)	0 vs 0 (NS)
Inabnet et al. [55]	22	Lateral transabdominal	NR	5.5 vs 6.1 (NS)	146 vs 153 (NS)	4.1 vs 4.6 (NS)	11 vs 8 (NS)	0 vs 9 (NS)	0 vs 0 (NS)
Sprung et al. [63]	34	Lateral transabdominal	100 vs 400 (<0.001)[a]	3 vs 7.5 (<0.001)[a]	177 vs 196 (0.3)	NR	0.5 vs 1 episode (0.41)	0 vs 0 (NS)	0 vs 0 (NS)
Mobius et al. [56]	18	Lateral and supine transabdominal	NR	6 vs 10 (<0.01)[a]	243 vs 100 (<0.01)[b]	3.8 vs 4.5 (NS)	7 vs 8 episodes (NS)	11 vs 0 % (NS)	0 vs 0 (NS)

The first value in each box reflects laparoscopic outcomes and the second open surgery outcomes

EBL estimated blood loss, *OR* operating room, *NS* not significant, *N*R not recorded

[a] Statistically significant, favoring laparoscopic procedure

[b] Statistically significant, favoring open procedure

Table 3 Transabdominal lateral approach

Author (year)	No. of patients	Return to OR % (etiology)	Infections (wound and intraabdominal) (%)	Conversion to OP % (etiology)	EBL ml (% > 500 ml or transfusion)	LOS (days)	OR time min (delay factors)	Time to oral intake (days)	Other complications
Berber et al. [7]	69	NR	NR	2.9	35	2	157	NR	2.9 %
Castillo et al. [8]	227	NR	NR	0.4	75 (2.2)	2.5	75 (S)	NR	4.7 % Intra-op 2.6 % Post-op
Gagner et al. [1]	97	1 (B)	NR	3 (O)	70 (2)	2.4	123	NR	10 %
Gil-Cardenas et al. [164]	100	NR	NR	5	2 (T)	5.0	174 (E)	NR	3 %
Henry et al. [5]	169	1.2 (B)	NR	5 (B, O)	1.2	5.4		NR	2.4 %
Kazaryan et al. [10]	242	NR	NR	NR	79 (1.2)	2.0	95 (P, C)	1.0	2.0 % Intraop
Kwan et al. [11]	353	NR	NR	4.5	50	6.8 (C)	153	NR	NR
Lee et al. [26]	358	1.4	0	NR	(0.1)	4.1	174	NR	3.6 %
Liao et al. (needlescopic) [12]	112	NR	1.8	NR	30 (0.9)	3.8 (C)	151 (P, M, A)	NR	1.8 %
Meria et al. [14]	212	NR	0	14 (B, A, FP, E)	85 (2.8)	3.6	102	0.9	4.7 % Vascular 10 % Postop
Meyer-Rochow et al. [16]	191	NR	NR	3.8 (B, O)	NR	3.9	161 (P)	NR	NR
Morris et al. [27]	246	0.4	1.2	3.7 (B, A, O, S)	67 (1.6)	2.2	160	NR	6.5 % 2 % Intraop
Nau et al. [28]	102	NR	NR	5 (P)	230	2.9	135	1.0	2.9 %
Nocca et al. [18]	120	NR	0.8	1.6	(3.3)	2.5	NR	NR	3.3 %
Parnaby et al. [29]	101	NR	3	5.9 (O, A, S)	(2)	2–3	120–132	NR	3 %
Shen et al. [20]	456	NR	NR	5.5 (A, B, O E, S, BMI)	NR	NR	NR	NR	NR
Soon et al. [21]	147	NR	NR	4.8 (B, O)	(2)	NR	154–198	NR	5.4 %
Terachi et al. [22]	311	NR	1.3	3.2 (B)	(1)	NR	NR	NR	8 % Vascular 4.2 % Other
Toniato et al. [35]	167	NR	NR	4.8	136–162 (3)	4.3–4.6	90–100 (C)	2.1	1.4 %
St Peter et al. (pediatric) [30]	140	NR	NR	9.9 (O, A)	(1.4)	NR	130	NR	0.7 %
Overall	4,425	0.4–1.4	0–3	0.4–14	Variable	2–6.8	75–198	0.9–2.1	0.7–14.7 %

Laparoscopic adrenalectomy outcomes based on technique

OR operating room, *OP* open procedure, *EBL* estimated blood loss, *LOS* length of stay, *NR* not recorded, *S* size of adrenal gland, *B* bleeding, *O* oncologic concerns, *T* transfusion, *E* improvement with experience, *P* pheochromocytomas, *C* Cushing's disease, *M* male, *A* adhesions, *FP* failure to progress, *BMI* high body mass index

the lateral decubitus position used during this approach affords excellent exposure because gravity pulls the abdominal contents outside the operating field. During left adrenalectomy, mobilization of the spleen medially is facilitated by LTA.

Relevant technical details

Patients are positioned at a 60° to 90° angle with the tumor side up and the table flexed for maximal opening of the space between the tip of the 12th rib and the iliac crest. Although variable, port positioning aims to establish instrument triangulation. The procedure usually can be accomplished with three ports for left adrenalectomy and four ports for right adrenalectomy (the fourth port is used for liver retraction).

During left adrenalectomy, the procedural steps include taking down the splenic flexure of the colon, freeing the splenic ligaments to mobilize the spleen and rotate it medially, dissecting in the avascular plane between the tail

Table 4 Posterior retroperitoneoscopic approach

Author (year)	No. of patients	Return to OR (%)	Wound infection (%)	Conversion to OP % (reason)	EBL ml (% > 500 ml or transfusion)	LOS (days)	OR time Min (delay factors)	Other complications
Barczynski et al. [163]	97	1.1	NR	8.2 (FP)	50	3	100 (E, S, P, M)	4.1 %
Berber et al. [7]	90	NR	NR	2.2	25	1	138	NR
Dickson et al. [9]	118	0	1.6	5.6 (W, E, BMI)	16 (2.4)	NR	114 (M, BMI)	7.2 %
Terachi et al. [22]	59	NR	NR	5.1	(1.7)	NR	NR	12 % Intra-op 1.7 % Post-op
Walz et al. [23]	560	0.18	0.05	2.0 (A, BMI, FP)	10 (0.8	NR	67 (E, M)	1.7 %
Overall	968	0–1.1	0.05–1.6	2–8.2	Variable	1–3	67–138	1.7–12 %

Laparoscopic adrenalectomy outcomes based on technique

OR operating room, *OP* open procedure, *EBL* estimated blood loss, *LOS* length of stay, *NR* not recorded, *FP* failure to progress, *E* improvement with experience, *S* size of adrenal gland, *P* pheochromocytomas, *M* male, *W* difficult working space, *BMI* high body mass index, *A* adhesions

Table 5 Lateral retroperitoneoscopic approach

Author (year)	No. of patients	Return to OR	Wound infection (%)	Conversion to OP (%)	EBL (ml)	LOS (days)	OR time (min)	Time to orals (days)	Other complications (%)
Fu et al. [3]	212	NR	1	NR	22	4.1	42	NR	NR
Lin et al. [13]	195	2 B	1.5	NR	68	4.5	93	2.1	2
Zhang et al. [25]	824	NR	0.25	0.12	25	5.6	45	1.2	NR
Overall	1,231	2	0.25–1.5	0.12	22–68	4.1–5.6	42–93	1.2–2.1	2

Laparoscopic adrenalectomy outcomes based on technique

OR operating room, *OP* open procedure, *EBL* estimated blood loss, *LOS* length of stay, *NR* not recorded

Table 6 Robotic lateral approach

Author (year)	No. of patients	Wound infection (%)	Conversion to OP % (etiology)	EBL (% > 500 ml)	LOS (days)	OR time min (delay factors)	Other complications (%)
Brunaud et al. [83]	100	2	5 (B)	NR	6.4	99 (E)	8
Nordenstrom et al. [85]	100	NR	7 (B, A, BMI, S)	4	NR	10 (E, M)	8
Overall	200	2	5–7	4	6.4	99–106	8

Laparoscopic adrenalectomy outcomes based on technique

OP open procedure, *EBL* estimated blood loss, *LOS* length of stay, *OR* operating room, *B* bleeding, *NR* not recorded, *NR* not recorded, *E* improvement with experience, *A* adhesions, *BMI* high body mass index, *S* size of adrenal gland, *M* male

of the pancreas and kidney, and controlling or dividing the adrenal vein as it enters the left renal vein. During right adrenalectomy, the procedural steps include mobilization of the right triangular ligament of the liver, an incision between the retroperitoneal attachments of the right lobe of the liver and the lateral border of the inferior vena cava (IVC), dissection of the lateral edge of the IVC, and taking of the right adrenal vein at the takeoff from the IVC. Retraction of the liver must be maintained by the assistant throughout the case to aid exposure of the right adrenal. Mobilization of the gland follows a superolateral to medioinferior progression unless the surgeon prefers taking the adrenal vein early, in which case an inferior to superior and medial to lateral mobilization of the gland is preferred.

Posterior retroperitoneoscopic adrenalectomy

Brunt et al. [73] first described the concept of posterior retroperitoneoscopic adrenalectomy (PRA) in a porcine model in 1993. During the next decade, Walz et al. [74] perfected the technique, demonstrating its safety and enhanced visualization with the use of higher insufflation pressures in the retroperitoneal cavity.

Advocates of PRA cite the advantage of direct access to the adrenal gland that avoids the intraabdominal cavity, making it attractive in the setting of prior abdominal surgery [7, 75]. Additionally, because the prone position facilitates equal access to the right and left sides, bilateral procedures performed by PRA do not require repositioning between sides [2, 9, 70]. The disadvantages include lack of access to the intraabdominal cavity for evaluation, difficulty removing large tumors and increased difficulty with increasing body mass index (BMI) due to the large distance between the gland and the skin, decreased working space from the additional fatty tissue, and occasionally, high peak airway pressures due to the prone position [9, 74]. Studies comparing PRA with other laparoscopic approaches have demonstrated a small yet significant benefit in pain medication requirement, time to oral intake, length of hospital stay, and overall convalescence with PRA (Table 4) [7, 22, 71, 72, 76–79].

Relevant technical details

Patients are positioned on a rectangular support with hip joints bent at a 90° angle, allowing the abdominal contents to fall forward with gravity, with the table flexed for maximal opening of the space between the 12th rib and the iliac crest. Three trocars, used for both the right and left procedures, are placed just under the 12th rib with a combination of direct palpation and finger guidance after the dorsal lumbar fascia has been digitally perforated.

With a balloon trocar positioned in the middle port, the retroperitoneal space is insufflated with 20–30 mmHg of carbon dioxide (CO_2). This high-pressure insufflation starts the dissection of the space, which is completed with blunt dissection of the area underneath the diaphragm and the fatty tissue above the superior border of the kidney. Landmarks that should be identified are the superior pole of the kidney caudally, the paraspinous muscles medially, and the posterior surface of the liver (right) or the spleen (left) laterally.

Dissection of the adrenal gland is facilitated by maintaining downward retraction of the kidney and starts inferiorly in a plane close to the kidney surface. The adrenal gland then can be elevated, allowing identification and ligation of the adrenal vein in a medial or inferomedial position with either clips or a hemostatic device. Mobilization of the gland is completed by dissecting laterally between the diaphragm and the psoas. The superior attachments are divided last. An important aspect of the procedure is having the first assistant maintain the horizon of the camera throughout the case.

Anterior transabdominal adrenalectomy

Anterior transabdominal adrenalectomy is a submesocolic approach and the least common of the techniques used for adrenalectomy. The main appeal is the conventional abdominal laparoscopic view familiar to all general surgeons [19, 80]. However, the operating times are generally longer, and a greater number of ports are needed for a successful operation.

Relevant technical details

With the patient in the supine position, a camera port is placed at the umbilicus, and three additional ports are placed in various configurations. The key steps for left adrenalectomy include elevating the transverse mesocolon, identifying the ligament of Treitz and the inferior mesenteric vein (IMV), and opening the posterior retroperitoneum lateral to the IMV. By dissecting inferior to the pancreas and elevating it, the left renal vein can be identified and followed to the left adrenal vein. After the vein is taken, the gland can be mobilized from inferior and medial to superior and lateral.

Lateral retroperitoneoscopic adrenalectomy

Lateral retroperitoneoscopic adrenalectomy (LPA) is the most common technique used by urologic surgeons for adrenalectomy, likely due to their familiarity with the anatomy of laparoscopic nephrectomy. Similar to PRA, LPA is advocated for patients with prior abdominal surgery [13, 76]. Although tumor size also is an important consideration in LPA, it does not seem to be as important as in PRA [24, 25]. Typically, the procedure has slightly longer operating times and requires more ports than LA or PRA but maintains the advantages of avoiding the peritoneal cavity as in PRA (Table 5) [22, 81].

Relevant technical details

The patient is positioned in a 60°–90° angle with the tumor side up and the table is flexed much the same as for the lateral transabdominal approach. However, four or five trocars are needed to complete the procedure on either side. The landmarks that should be identified during the procedure are the superior pole of the kidney, the parietal peritoneum, the diaphragm, the retroperitoneal fold, the posterior renal fascia, and the psoas muscle. The retroperitoneal fat outside both Gerota's fascia and the posterior renal fascia must be cleared from below the diaphragm to the iliac fossa until the fat prolapses into the fossa. A longitudinal incision in Gerota's fascia near the diaphragm facilitates dissection in three key planes: between the perirenal fat and the anterior renal fascia under the diaphragm, between the perirenal fat and the posterior fascia on the lateral upper pole of the kidney, and between the adrenal gland and the upper pole of the kidney. As in PRA, mobilization begins inferior to the gland along the superior border of the kidney, and elevation of the gland facilitates further mobilization, with division of the superior attachments last.

Recommendations

Several approaches to LA have been described in the literature. Surgeons should choose the approach most familiar to them, the one for which they have been trained, and the one that has the best patient outcomes (+++, strong). Surgeons also should take into consideration that in specific clinical circumstances, some approaches may be more beneficial than others:

- For patients with previous abdominal surgery, a retroperitoneal approach may be associated with a shorter operative time and fewer complications (++, weak).
- For bilateral adrenalectomies, the posterior retroperitoneal approach may be advantageous because it eliminates patient repositioning during the case (++, weak).
- For morbidly obese patients (BMI >35 kg/m^2) and for large tumors (>6 cm), the lateral transabdominal approach may increase the feasibility of the procedure compared with the other approaches (++, weak).

Robotic adrenalectomy

Since the first robotic adrenalectomy (RA) by Horgan and Vanuno [82] in 2001, several other groups have successfully adopted the robotic approach. Brunaud et al. [83, 84] has reported the largest series of lateral transabdominal RA to date, showing that after a learning curve of 20 cases, the main predictors of operative time in RA are tumor side, previous clinical experience, and the first assistant's skill. These authors also reported that RA might be especially useful for patients with a high BMI (>30–35 kg/m^2) and for large tumors (>5.5 cm). Similarly, Nordenstrom et al. [85] has reported advantages for obese patients and for large tumors in their series with robotic RPA (Table 6).

Proponents of the robotic technique cite the advantages of three-dimensional depth perception, the added element of dexterity with the "wrist" action of robotic instruments, and superior ergonomic conditions for the surgeon [86]. The main disadvantages addressed by most authors are cost and the learning curve for the entire surgical team [84, 85, 87, 88].

From a technical aspect, all authors stress the importance of training an entire operative team. For lateral RA, the robotic setup is an extreme flank position with the robotic camera axis above and lateral to the umbilicus. The robotic cart is positioned at a 45° angle to the table over the head of the patient, with the working axis of the robot directed toward the ipsilateral clavicle [83, 89]. For retroperitoneal RA, the table is rotated 30° clockwise, with the robot brought in from the head and positioned between the shoulders [85, 90].

Recommendations

Compared with standard laparoscopic techniques, RA may offer advantages for large tumors and morbidly obese patients (+, weak). However, given the increased cost, longer operative times, and lack of clear patient outcome benefits using this technique, additional higher-quality evidence is needed before a firm recommendation can be provided.

Single-port adrenalectomy

Outcomes with single-incision adrenalectomy have been reported recently by several authors [91–95]. Published nonrandomized series comparing conventional laparoscopic approaches and single-port adrenalectomy have demonstrated no significant differences in patient hospital lengths of stay or morbidity and a small benefit in cosmesis and postoperative pain but longer operative times with single-port laparoscopy [96–98].

From a technical standpoint, a transabdominal single-port adrenalectomy requires a 2- to 3-cm incision for a multiport device. Placement of the device at the umbilicus has been described, which requires extra-long instruments to reach the adrenal gland and underneath the 12th rib for a more direct, although less cosmetic, location. For right adrenalectomies, an additional 2-mm needlescopic port is needed for liver retraction. With a retroperitoneal approach, specific recommendations regarding the multiport include placing the camera in the lower aperture position and using ports of different lengths [96, 97]. Additionally, Walz et al. [97] described the need for a more extended mobilization of the upper pole of the kidney than with his conventional retroperitoneal approach.

Recommendations

Based on the available evidence, single-port adrenalectomy is feasible and safe when undertaken by an experienced surgeon but offers little if any advantage over other standard laparoscopic approaches to adrenalectomy. Additionally, better-quality evidence is needed before this approach can be recommended (+, weak).

Partial adrenalectomy

The first modern clinical use of cortical-sparing adrenalectomy was described by van Heerden et al. [99] for the treatment of bilateral hereditary pheochromocytomas in

1985. During the past 25 years, with hopes of sparing patients from lifelong steroid dependence and the complications of adrenal insufficiency, laparoscopic partial adrenalectomies have replaced bilateral adrenalectomies for hereditary pheochromocytomas. Recently, cortical-sparing operations for unilateral functional tumors have been reported [3, 81, 100]. Perioperative outcomes using this technique do not differ from those of complete adrenalectomy. Studies reporting long-term outcomes after partial adrenalectomy have shown steroid-free outcomes for up to 91 % of patients [14, 70, 100–102].

The literature shows general agreement that the location of the tumor within the gland is the main determinant of the ease and ability to perform a partial adrenalectomy. Tumors anterior to the gland and on its margin generally are more amenable to partial removal than those on the its posterior surface. In the LA and open adrenalectomy (OA) literature, the reported amount of adrenal cortical tissue needed to preserve adrenal function is one-third of one gland or 15 % of the total adrenal cortical tissue [70, 103–105]. In preparation of the remnant, it is suggested that the portion of adrenal cortex to be preserved should not be mobilized out of the retroperitoneum to preserve the blood supply and that all tumors should be resected with a 0.5- to 1-cm margin of normal adrenal tissue [104, 106]. Preservation of the adrenal vein is not essential and depends on the situation [2, 3, 81, 101]. Additionally, liberal use should be made of laparoscopic ultrasound because it is a useful adjunct for showing clear differentiation of the tumor from normal tissue [2, 89, 101, 104, 107]. It also should be noted that except in the case of partial adrenalectomy, experts generally recommend extracapsular dissection with preservation of the capsule of the adrenal gland and resection of the surrounding fatty tissue during removal of the adrenal gland.

Recommendations

Partial adrenalectomy is safe and feasible in the hands of appropriately trained surgeons. For patients requiring bilateral adrenalectomy (e.g. for hereditary pheochromocytomas), laparoscopic cortical-sparing surgery may be the procedure of choice (++, weak). Additional evidence is needed before a recommendation can be provided for partial adrenalectomy of single-gland, nonhereditary tumors.

Method and timing for taking the adrenal vein

For many years, surgeons learning the technique of OA were taught to take the adrenal vein early, especially in managing pheochromocytomas, to prevent catecholamine release during surgery that could affect the patient's hemodynamic parameters and potentially their outcomes. However, with the introduction of laparoscopic surgery, a significantly lower catecholamine surge has been described to occur [108]. This is believed to result from the more gentle dissection and decreased gland manipulation when the surgery is performed by an experienced laparoscopic surgeon. In addition, recent studies have demonstrated no difference in outcomes when the adrenal vein is taken first versus last or not at all during partial adrenalectomies [101, 109, 110].

For vein control, most surgeons use metal clips, although other hemostatic devices such as ultrasonic shears, the Ligasure device (Ligasure™, Covidien, Boulder, CO), or electrothermal bipolar systems also have been used successfully. Comparative studies on the preferred type of vein control device are lacking [87, 97, 111, 112].

Recommendations

The classic teaching for early vein control during OA has not been confirmed for LA because patient outcomes do not appear to be affected by early versus late ligation. Thus, the type and timing of adrenal vein control depends on surgeon preference and the specific anatomic variables associated with each case (+, weak).

Laparoscopic adrenalectomy for suspected or proven adrenal cortical carcinoma and adrenal metastases

Published data comparing LA and OA for adrenal cortical carcinoma (ACC) are limited. Advocates for an open approach cite the higher rates of local and peritoneal recurrences in the laparoscopic group, the shorter time to recurrence, and the higher incidence of positive margins [4, 113, 114]. Advocates for LA argue that for stages 1 and 2 ACC tumors, LA has outcomes similar to OA when performed in a large-volume referral center with surgeons strictly adhering to standard oncologic principles [18, 115, 116].

Many surgeons argue that for medium and large incidental tumors without a preoperative indication of malignancy, it is appropriate to start the procedure laparoscopically, but the surgeon needs to convert to open surgery when signs of tumor adhesion or invasion, enlarged lymph nodes, or a difficult dissection is encountered [5, 6, 117]. The Third International Adrenal Cancer Symposium highlighted the limitations of the available literature and concluded that the most important variables for good patient outcomes were an appropriate oncologic resection and treatment at a specialized center [115].

Recommendations

For ACC, the best determinant of patient outcomes is an appropriate oncologic resection that includes en bloc resection of any contiguous involved structures and regional lymphadenectomy. Thus, an open approach to resection may be best. If a laparoscopic approach is chosen (due to an unknown malignancy status preoperatively or suspected early-stage ACC), conversion to open surgery is strongly recommended when difficult dissection is encountered due to tumor adhesion or invasion or enlarged lymph nodes are seen (++, strong).

Adrenal metastases

Laparoscopic resection of metastases to the adrenal gland is being performed in increasing numbers due to two concurrent developments. First, is the adoption of LA as the standard of care for benign adrenal tumors because of the shorter hospital stay, quicker recovery, less blood loss, and overall lower morbidity. Second, the last few decades have seen an overall improvement and evolution of cancer treatment in general. Patients live longer with their disease, and more recurrences are limited to a single site.

Before laparoscopy, the risks and morbidity associated with an adrenalectomy performed for a solitary cancer metastasis did not generally appear to outweigh the benefits. However, in the past 15 years, the scales have tipped in favor of laparoscopic resection.

Laparoscopic resection of a solitary adrenal metastasis in a patient with an otherwise controlled cancer is a safe procedure with a very low morbidity rate that seems to have long-term outcomes similar to those of open surgery in the few selected published series [32–34, 118–124]. The most common cancers that metastasize to the adrenal gland are lung, breast, kidney, melanoma, gastrointestinal cancer, and lymphoma.

The largest study that directly compared laparoscopic with open resection of metastases reported on 94 patients with up to 31 months of follow-up evaluation [34]. In this series, the patients who underwent laparoscopic resection had shorter operative times, shorter hospital stays, less blood loss, and lower overall morbidity rates (including laparoscopic conversions). However, they had rates of positive resection margins, local and overall recurrence, and disease-free survival similar to those of open resection. Three other small studies that also compared laparoscopic with open resection reported similar results [118, 120, 123].

Recommendations

Solitary metastases to the adrenal gland without evidence of local invasion can be approached laparoscopically by a surgeon skilled in advanced laparoscopy and adrenal surgery (+, weak). If local invasion is found intraoperatively, conversion to an open approach is warranted (+, strong).

Laparoscopic adrenalectomy for large adrenal masses

The use of laparoscopy for excision of large adrenal tumors is debated, and the literature on the subject is scant and retrospective in nature. As discussed in the section on LA performed for suspected or adrenal cortical carcinoma, an open approach is recommended for patients with known or probable primary adrenal cortical carcinoma. Conversion from a laparoscopic to an open approach also is recommended for cases with intraoperative signs of carcinoma such as tumor adhesions, local invasion, enlarged lymph nodes, or a difficult dissection. The question of how to approach large adrenal tumors (>5–6 cm) with no pre- or intraoperative evidence of malignancy, however, is a dilemma to the surgeon.

The overall safety of laparoscopy for large tumors without evidence of carcinoma has been reported in several small series [8, 29, 125–130]. In general, the outcome of LA for large tumors is similar to that for small tumors in terms of operating room time [29, 128, 129], hospital stay [29, 128–130], and complication rate [29, 128, 130], but findings have shown a tumor size of 7.5 cm or larger to be an independent risk factor for a longer operating time, more blood loss [8, 127, 128], a longer hospital stay [8], and a higher rate of conversion to open surgery [29]. A shorter operating room time has been reported among patients undergoing LA for tumors smaller than 5 cm compared with tumors larger than 5 cm [130].

Recommendations

Large adrenal tumors without pre- or intraoperative evidence of primary adrenal cortical carcinoma can be approached laparoscopically by a surgeon skilled in advanced laparoscopy and adrenal surgery (+, weak). Laparoscopic adrenalectomy for larger tumors may be associated with a longer operating room time, more blood loss, and a higher rate of conversion to open surgery (+, weak). If any evidence for carcinoma is found intraoperatively, conversion to an open approach is warranted (should be strongly considered) (+, strong).

Pheochromocytoma

Despite early concerns regarding perioperative cardiovascular complications related to pneumoperitoneum, organ manipulation, and dissection, a number of published series have demonstrated laparoscopic management of pheochromocytomas to be safe and effective [56, 108, 131]. Nevertheless, compared with other adrenal pathologies, minimally invasive adrenalectomy for pheochromocytoma, even for experienced surgeons, still can be associated with longer operative times, more blood loss, increased complications, and longer hospital stays [132]. The following sections highlight a number of important considerations for surgeons who care for patients with pheochromocytoma.

Preoperative care

For patients with preoperative signs, symptoms, and biochemical evidence of catecholamine excess, alpha-adrenergic blockade should be initiated at least 10 days before surgery. Phenoxybenzamine has historically been considered the gold standard for preoperative alpha blockade. An initial dose of 10 mg administered orally twice a day can be titrated upward with regimens of 10–20 mg three times a day to provide adequate blockade in most patients, particularly when combined other antihypertensive agents that most patients are receiving at baseline.

Phenoxybenzamine is a long-acting alpha antagonist, and its use in higher doses has been associated with frequent side effects including nasal congestion, nausea, abdominal pain, and tachycardia. Consequently, many surgeons and endocrinologists have transitioned to the use of shorter-acting alpha blockers such as doxazosin, which tend to have fewer side effects. In addition, more rapid metabolism tends to translate into less postoperative hypotension related to residual unopposed alpha blockade [133, 134]. Some authors also have advocated the combined use of alpha blockers with metyrosine, which inhibits tyrosine hydroxylase, the rate-limiting step in catecholamine synthesis. Early data suggest that this combination may limit intraoperative hemodynamic instability to a greater degree than alpha blockade alone [135, 136].

The clinical end point for preoperative blockade is control of hypertension. Adequate preoperative alpha blockade can be confirmed by increasing the dosage until the patient experiences mild orthostatic hypotension. For patients who also experience tachycardia or arrhythmias, the addition of a beta-adrenergic blockade should be initiated only after adequate alpha blockade has been achieved. Patients with alpha blockade-induced orthostatic hypotension should be treated with oral or intravenous volume loading before surgery. All patients should also be given 1–2 l of intravenous crystalloid solution for intravascular volume expansion before induction of general anesthesia the day of surgery [137–142].

Recommendations

Before LA for pheochromocytoma, alpha-adrenergic receptor blockade should be considered for all patients. When used preoperatively, alpha blockade should be continued until signs of orthostatic hypotension are evident (+++, weak). Short-acting alpha blockers may be preferable to long-acting ones. Beta blockade also should be considered for appropriately selected patients and instituted only after adequate alpha blockade (++, weak).

Intraoperative management

Careful perioperative monitoring of hemodynamic status is critical to the safe resection of catecholamine-producing tumors. Before the induction of general anesthesia, an arterial line should be placed. A central venous line also is recommended for infusion of vasoactive drips and monitoring of volume status.

Despite appropriate preoperative medical management, intraoperative hypertension is common and represents a valid concern. Continuous invasive monitoring and pharmacologic intervention by an experienced anesthesia team are necessary to avoid substantial cardiovascular instability. Drips should be prepared and ready to infuse at any point during the procedure. Hypertension generally is treated with nitroprusside, nitroglycerine, or nicardipine. Tachyarrhythmias can be managed with intravenous beta blockers or lidocaine [142].

After ligation of the adrenal vein and removal of the tumor, significant hypotension can develop precipitously. Hypotension is treated with volume resuscitation and alpha-adrenergic agonists such as vasopressin. Depending on the degree of residual alpha blockade, some patients require pressor support after surgery.

In addition to relying on pharmacologic manipulation in the treatment of intraoperative hypertension, the surgeon can use a number of strategies to minimize dramatic fluctuations in blood pressure during resection of pheochromocytomas. By avoiding excessive tumor manipulation, the effects of catecholamine surges can potentially be mitigated.

During both OA and LA, findings have shown tumor manipulation to be the most significant intraoperative stimulus for catecholamine release. Clinically, sudden increases in plasma catecholamine levels can result in episodes of dramatic and dangerous intraoperative hypertension that can be difficult to control even with rapid infusion of vasodilators. Intraoperative catecholamine monitoring has demonstrated that mean plasma epinephrine and norepinephrine levels can increase up to 34-fold during tumor manipulation [143–146]. Careful adrenal dissection and tumor handling are important strategies for avoiding catecholamine-induced cardiovascular instability. These techniques require that the surgeon minimize direct manipulation or compression of the gland itself. In many cases, adjacent structures such as the kidney, pancreas, and liver can be dissected and retracted away from the tumor, and periadrenal fat or Gerota's fascia can be used as a handle such that the gland can be manipulated without actual placement of direct pressure on the tumor.

As mentioned earlier in these guidelines, early ligation of the adrenal vein is not necessary during pheochromocytoma resection because it has not been shown to have an impact on hormonal release by the tumor. On the other hand, intraabdominal insufflation during laparoscopic pheochromocytoma excision may cause an increase in serum catecholamines [147, 148]. Although the mechanism is unclear, the stimulus is thought to relate either to direct tumor compression or to a change in tumor perfusion. In addition, pneumoperitoneum with CO_2 may lead to hypercapnia and acidosis, which are known stimuli of catecholamine secretion and hypertension. As a result, helium has been suggested as an alternate insufflation agent to eliminate the deleterious effects of CO_2 during LA for pheochromocytoma. In a prospective evaluation of 11 patients undergoing helium insufflation during laparoscopic pheochromocytoma resection, the authors demonstrated that its use avoided significant intraoperative hypercarbia or acidosis and provided greater intraoperative hemodynamic stability [143]. These data have not been substantiated by a large prospective series, and given the overall safety of CO_2, most surgeons continue to use standard CO_2 insufflation.

In addition to the problems associated with catecholamine liberation, large size and prominent vascularity compound the challenges of removing pheochromocytomas. Compared with other indications for adrenalectomy, both laparoscopic and open resection of pheochromocytomas have been associated with longer operative times, higher complication rates, greater blood loss, and longer hospitalization in some selected series [1, 149]. In general, these tumors tend to be larger than other functional and nonfunctional adrenal lesions and often have a large number of arterial and venous tributaries that bleed with minimal manipulation. Generous use of clips in addition to vessel-sealing technology is advisable for reliable hemostasis.

Large tumors often encroach on the renal vessels, particularly on the left side. The renal vessels must be carefully identified and protected to avoid inadvertent injury during dissection. The need to operate around the renal hilum or to perform an en bloc resection of the periadrenal fat together with the adrenal gland does not mandate a conversion to laparotomy. However, conversion to an open procedure is warranted when laparoscopic dissection cannot be performed safely or a complete resection cannot be performed without undue trauma to the gland. In the setting of pheochromocytoma, this determination must be based on intraoperative findings of tumor invasion into adjacent structures because radiographic and histologic information, including intraoperative frozen section examination, are unreliable predictors of malignancy [150, 151].

Recommendations

Invasive hemodynamic monitoring should be considered during LA for pheochromocytomas (++, strong). To minimize hemodynamic instability due to catecholamine release during surgery, minimization of direct manipulation or compression of the adrenal gland is necessary (++, strong). Early ligation of the vein does not prevent hemodynamic instability (+, weak). Due to the added challenge of intraoperative hemodynamic variability, frequent communication between the surgical and anesthesia teams is important for optimal perioperative outcomes.

Postoperative management

During the immediate postoperative period, hypotension and hypoglycemia are the most common occurrences. Monitoring in an intensive care unit (ICU) setting for 24 h postoperatively is advisable. The need for pressors or antihypertensive therapy postoperatively is dictated by the patient's hemodynamic status. For patients without evidence of underlying postoperative essential hypertension, all antihypertensive medications should be discontinued postoperatively with the possible exception of beta blockers. For patients who have been treated with long-term preoperative beta blocker therapy, postoperative management may necessitate a slow taper to avoid reflex tachycardia.

Because no definitive diagnostic criteria exist for malignancy in pheochromocytoma and because the true malignant potential of pheochromocytomas is very difficult to predict, patients require long-term follow-up evaluation to confirm the absence of recurrence.

The recurrence rates in the literature after resection of benign-appearing lesions are approximately 6–8 %, and long disease-free intervals are not atypical, with recurrences often presenting several years to decades after initial surgery [150–154]. Thus, follow-up recommendations include annual blood pressure monitoring as well as plasma and/or urinary metanephrines. For patients who demonstrate clinical signs or symptoms of recurrence, abdominal imaging is indicated [155]. Common histologic features, such as capsular invasion, vascular and lymphatic penetration, nuclear atypia, and mitotic activity, which almost always indicate malignancy in other tumors, do not always indicate malignancy in pheochromocytomas, nor does the lack of these pathologic features dictate that a tumor is benign.

In 2002, a pheochromocytoma of the adrenal gland scaled score (PASS) was developed based on various degrees of cytologic atypia including invasion, necrosis, cellularity, mitoses, pleomorphism, and growth. A PASS score of 4 or higher indicated an aggressive pathology

[156]. However, although the utility of PASS was replicated in one large cohort, other smaller studies did not find the PASS score to be useful for predicting further malignancy and advocated for its further refinement [157–160].

Additionally, two recent papers have indicated that tumor size, location, and urinary vanillylmandelic acid levels are important features for anticipating tumor recurrence [161, 162]. Thus, it appears that individual tumor biology rather than the surgical approach may determine the chances of cure. Nonetheless, extreme care must be taken to avoid intraoperative capsular disruptions and possible iatrogenic pheochromocytosis because small case reports have described early local recurrence of pheochromocytoma after initial laparoscopic resection and tumor spillage. In that same context, adrenal specimens removed with minimally invasive techniques should be placed in an impervious extraction bag before removal, morcellation, or both.

Recommendations

Due to the potential for hemodynamic instability after pheochromocytoma resection, all patients should be closely monitored in the early postoperative phase (++, strong). Capsular disruptions of the adrenal gland during surgery should be avoided to minimize the risk of disease recurrence (+, weak). Given the lack of clear predictors of malignancy to detect recurrences, patients with pheochromocytoma should be monitored long term with annual blood pressure measurements, plasma and/or urinary metanephrine levels, and, if indicated, also abdominal imaging (++, strong).

Learning curve

The laparoscopic literature clearly shows that extensive experience of the surgeon and surgical team optimizes patient outcomes and cost effectiveness in the operating room. For LA and RA, the learning curve appears to be 20–40 cases [1, 5, 23, 83, 153, 163]. In general practice, this number may be difficult to achieve due to the paucity of these procedures. Controversy exists as to which approach, anterior or posterior, requires more cases for the surgeon's operative time and the patient's morbidity to plateau [76–78]. Nevertheless, learning curve comparisons between different surgical approaches are difficult because other factors such as the surgeon's previous experience and the operative team's familiarity and pre-implementation training also significantly influence the procedure learning curve [75, 109, 152].

Recommendations

Minimally invasive adrenalectomy is associated with a learning curve that may be difficult to overcome given the paucity of these cases in general practice. Dedicated, advanced training should be pursued by surgeons unfamiliar with this technique. Until proficiency with LA is attained, referral to a center with expertise in minimally invasive adrenal surgery should be considered (++, strong).

Limitations of the available literature

The available literature on LA has several limitations. Few small controlled trials are available, and most studies are retrospective in nature, with significant heterogeneity among them and increased risk for publication bias as well as other confounding factors. In addition, reporting of outcomes varies significantly, as does the follow-up period, which generally tends to be short, making it difficult to combine and compare such data. Finally, most of the studies do not report details on the expertise of their surgeons, and most have been conducted in a single institution, making the generalization of their findings difficult. Due to these limitations of the literature, firm recommendations are difficult.

Summary of recommendations

1. Minimally invasive adrenalectomy is associated with less postoperative pain, a shorter hospital stay, earlier recovery, and similar long-term outcomes compared with open surgery and has been established as the preferred approach for all nonprimary adrenal cancer pathology (+++, strong).
2. Several approaches to LA have been described in the literature. Surgeons should choose the approach most familiar to them, which they have been trained to perform and which has shown the best patient outcomes (+++, strong). Surgeons also should take into consideration that in specific clinical circumstances, some surgical approaches to adrenalectomy may be more beneficial than others:
   - For patients with previous abdominal surgery, a retroperitoneal approach may be associated with a shorter operative time and fewer complications (++, weak).
   - For bilateral adrenalectomies, the posterior retroperitoneal approach may be advantageous because it eliminates patient repositioning during the case (++, weak).
   - For morbidly obese patients (BMI >35 kg/m^2) and for large tumors (>6 cm), the lateral transabdominal approach may increase the feasibility of the procedure compared with the other approaches (++, weak).

3. Compared with standard laparoscopic techniques, robotic adrenalectomy may offer advantages for large tumors and for morbidly obese patients (+, weak). However, given the increased cost, longer operative times, and lack of clear patient outcome benefits using this technique, additional higher-quality evidence is needed before a firm recommendation can be provided.
4. Based on the available evidence, single-port adrenalectomy is feasible and safe when undertaken by an experienced surgeon but offers little if any advantage over other standard laparoscopic approaches to adrenalectomy. Additional, better-quality evidence is needed before this approach can be recommended (+, weak).
5. Partial adrenalectomy is safe and feasible in the hands of appropriately trained surgeons. For patients requiring bilateral adrenalectomy (e.g. for hereditary pheochromocytomas), laparoscopic cortical-sparing surgery may be the procedure of choice (++, weak). Additional evidence is needed before a recommendation can be provided for partial adrenalectomy of single-gland, nonhereditary tumors.
6. The classic teaching for early vein control during OA has not been confirmed for LA because patient outcomes do not appear to be affected by early versus late ligation. Thus, the type and timing of adrenal vein control depends on surgeon preference and the specific anatomic variables associated with each case (+, weak).
7. For adrenocortical carcinoma, the best determinant of patient outcomes is an appropriate oncologic resection that includes en bloc resection of any contiguous involved structures and regional lymphadenectomy. Thus, an open approach to resection may be best. If a laparoscopic approach is chosen (due to unknown malignancy status preoperatively or suspected early-stage carcinoma), conversion to open surgery is strongly recommended when difficult dissection is encountered due to tumor adhesion or invasion or enlarged lymph nodes are seen (++, strong).
8. Solitary metastases to the adrenal gland without evidence of local invasion can be approached laparoscopically by a surgeon skilled in advanced laparoscopy and adrenal surgery (+, weak). If local invasion is found intraoperatively, conversion to an open approach is warranted (+, strong).
9. Large adrenal tumors without pre- or intraoperative evidence of primary adrenal cortical carcinoma can be approached laparoscopically by a surgeon skilled in advanced laparoscopy and adrenal surgery (+, weak). For larger tumors, LA may be associated with longer operating room times, greater blood loss, and a higher rate of conversion to open surgery (+, weak). If any evidence for carcinoma is found intraoperatively, conversion to an open approach is warranted (should be strongly considered) (+, strong).
10. Before LA for pheochromocytoma, alpha-adrenergic receptor blockade should be considered for all patients. When used preoperatively, alpha blockade should be continued until signs of orthostatic hypotension are evident (+++, weak). Short-acting alpha blockers may be preferable to long-acting ones. Beta blockade should also be considered for appropriately selected patients and instituted only after adequate alpha blockade (++, weak).
11. Invasive hemodynamic monitoring should be considered during LA for pheochromocytomas (++, strong). To minimize hemodynamic instability due to catecholamine release during surgery, minimization of direct manipulation or compression of the adrenal gland is necessary (++, strong). Early ligation of the vein does not prevent hemodynamic instability (+, weak). Due to the added challenge of intraoperative hemodynamic variability, frequent communication between the surgical and anesthesia teams is important for optimal perioperative outcomes.
12. Due to the potential for hemodynamic instability after pheochromocytoma resection, all patients should be closely monitored in the early postoperative phase (++, strong). Capsular disruptions of the adrenal gland during surgery should be avoided to minimize the risk of disease recurrence. (+, weak). Given the lack of clear predictors of malignancy to detect recurrences, patients with pheochromocytoma should be monitored long term with annual blood pressure measurements, plasma and/or urinary metanephrine levels, and if indicated, also abdominal imaging (++, strong).
13. Minimally invasive adrenalectomy is associated with a learning curve that may be difficult to overcome given the paucity of these cases in general practice. Dedicated, advanced training should be pursued by surgeons unfamiliar with this technique. Until proficiency with LA is attained, referral to a center with expertise in minimally invasive adrenal surgery should be considered (++, strong).

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