Adrenal-preserving Minimally Invasive Surgery: Update on the Current Status of Laparoscopic Partial Adrenalectomy

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Adrenalectomy is the standard of care for hormonally active adrenal masses. In recent years, minimally invasive laparoscopic excision has become a preferred management option. As with advances in parenchymal-sparing renal surgery, investigators have begun to examine adrenal-sparing procedures to preserve functional adrenal tissue. This article reviews the recent literature and reports on intermediate results with laparoscopic partial adrenalectomy (LPA).

Introduction

Laparoscopic adrenalectomy has emerged as the standard for surgical removal of the adrenal gland. First reported in 1992 by Gagner et al. [1,2], the laparoscopic technique is as safe and efficacious as the open approach, but it is associated with less pain, shorter hospitalization, and more rapid convalescence [1–3].

For patients requiring bilateral adrenalectomies, adrenal-sparing surgery may obviate life-long hormonal supplementation and reduce associated risks such as osteoporosis and hypoandrogenism. Addisonian crisis following bilateral adrenalectomy is reported in 25% to 33% of cases [4,5]. Adrenal-sparing procedures, therefore, may offer improved quality of life and reduced long-term morbidity.

We initially reported on the role of adrenal-sparing procedures in 2003, including laparoscopic partial adrenalectomy (LPA), cryoablation, and radiofrequency ablation [6]. Herein, we review the recent literature on LPA and discuss intermediate experience with the technique.

Laparoscopic Partial Adrenalectomy

Partial adrenalectomy was first proposed to preserve a maximal amount of adrenal tissue and spare patients from requiring chronic steroid replacement, which is particularly important in patients with bilateral benign adrenal tumors or a solitary adrenal gland, as well as in patients at risk for the development of multiple adrenal tumors, such as multiple endocrine neoplasia (MEN-2) and von Hippel–Landau (VHL) disease. After bilateral adrenalectomy, patients require chronic steroid replacement, which involves drawbacks including dose adjustment during stressful events and the possibility of overtreatment that results in damaging effects on bone and other potential complications of lifelong hormonal supplementation [7,8]. Most patients who undergo unilateral, total adrenalectomy have sufficient hormonal reserve not to require steroid replacement, yet investigators have noted suboptimal hormonal responses to stress in these patients [5,9]. Therefore, leaving as much normal adrenal tissue as possible may provide patients with more hormonal reserve; as such, researchers have begun to extend these techniques to sporadic unilateral tumors [8].

Adrenal adenoma

For the management of primary hyperaldosteronism due to aldosterone-producing adenomas (APA), laparoscopic total adrenalectomy is the standard treatment, even though only a small focus in the gland may be the source of aldosterone hypersecretion. When a patient is rendered with only a solitary adrenal gland, the contralateral gland then assumes the hormonal secretion workload. Should the adrenal gland require future excision or suffer functional impairment, the patient may lose the remaining source of steroid production. For this reason, partial adrenalectomy was proposed as a solution. Initial investigations of partial excision determined whether this procedure would offer a benefit. Nakada et al. [5] compared the outcome of open, unilateral, partial adrenalectomy with unilateral, total adrenalectomy in 48 patients with primary hyper-

aldosteronism. The study demonstrated that unilateral, total adrenalectomy preserved sufficient hormonal reserve in patients to avoid hormonal replacement, although hormonal response to stress was suboptimal [5]. The procedure was shown to be efficacious, with no instances of recurrent hyperaldosteronism in either group over 5-years mean follow-up. Further, partial adrenalectomy with enucleation of an adenoma seemed preferable, leaving patients with significant adrenal tissue and providing additional hormonal reserve.

In 1997, the initial report on LPA involved a patient with bilateral adrenal adenomas [10]. Via APA enucleation, the procedure was touted as simpler to perform than laparoscopic total adrenalectomy, and it was ultimately uneventful. At follow-up, the patient had normalization of split adrenal function tests. Since this report, preliminary case reports of transperitoneal and retroperitoneoscopic LPA showed that it was safe and effective to treat patients with adrenal adenomas [8,10–12]. More recently, the literature has included larger studies with longer follow-up, enabling technique refinement and discussion on potential indications [13–16].

In 2004, Walz et al. [17••] reported on 325 posterior retroperitoneoscopic adrenalectomies, including 100 partial adrenalectomies, the most reported LPAs performed for 30 aldosterone-producing adenomas, 33 pheochromocytomas, 20 cortisol-producing adenomas, and 17 nonfunctioning tumors. Mean tumor size was 2.8 ± 1.5 cm, mean operating time was 80 minutes, and mean blood loss was 29 mL; these results compare with total laparoscopic adrenalectomy. Tumors were resected using several modalities, including electrocautery, ultrasonic energy, or clips. Adhering to the reports of Brauckhoff et al. [18], Walz et al. [17••] state that preservation of the main adrenal vein is not essential, as maintaining at least one-third of the gland volume can preserve adrenal function. Maintenance of cortical function was preserved in 14 of 15 patients with bilateral adrenal tumors. In all 96 patients who underwent partial adrenalectomy, biochemical cure was proven, with no evidence of recurrence at 51 months' follow-up.

Additionally, Jeschke et al. [19] reported on 13 patients who underwent transperitoneal LPA for APAs with a mean diameter of 2.1 cm. Centrally located lesions were excluded, as well as lesions that had equivocal findings on CT scan. The authors avoided vascular stapler use. Instead, with intraoperative ultrasound, they employed a combination of bipolar energy and endoshears to excise a 2- to 3-cm margin around the tumor. After resection, application of fibrin glue to the resection line assisted with hemostasis. Contrary to Walz et al. [17••], adrenal vein preservation was essential to maintaining function of the remaining adrenal tissue. Mean operating time was 99 minutes, mean estimated blood loss was 78 mL, and mean hospital stay was 4.3 days. All margins were negative in this series, with histology confirming a single adenoma, and all patients had normal blood pressure and aldosterone levels at mean follow-up of 39 months, with no recurrences. For small, benign adrenal tumors, even in patients with a normal contralateral adrenal gland, this group routinely recommends LPA [19].

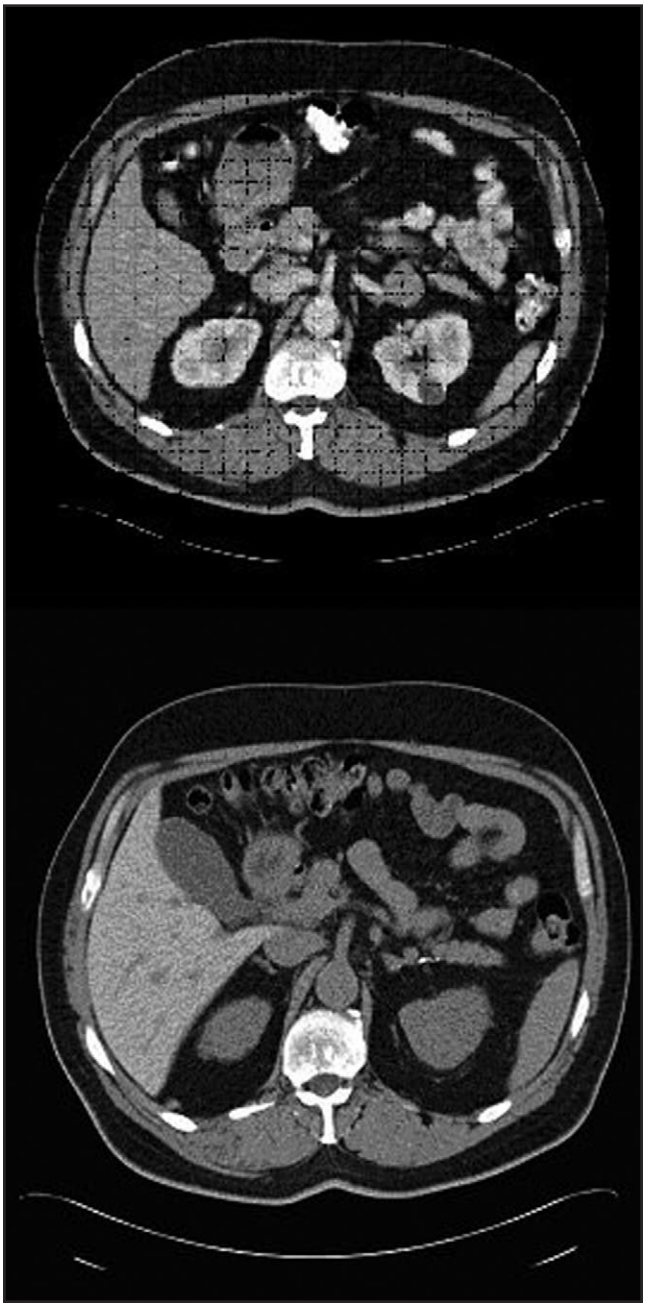

Figure 1. Preoperative CT demonstrating a left adrenal mass (*top*) and postoperative CT 3 months after left laparoscopic partial adrenalectomy (*bottom*).

At our institution, we have intermediate follow-up on three patients who underwent LPA for aldosterone-producing adenomas. Tumors measured 1.5 cm (right), 2.5 cm (right), and 5 cm (left) in size and were resected using the Harmonic Scalpel (Ethicon, Cincinnati, OH) or a vascular linear stapling device (Fig. 1). The adrenal vein was preserved in all cases. The mean age was 70 years (range,

61–83), operative time was 183 minutes, estimated blood loss was 93 mL, and length of hospital stay was 1.3 days. Following the procedure, serum aldosterone and potassium levels normalized in all patients. At mean follow-up of 52 months, each patient remained asymptomatic, with stabilization of blood pressure. Two patients required no antihypertensive medication and a third patient had greater than 75% reduction in antihypertensive medication requirement (one medication instead of five).

Such reports and our experience demonstrate the efficacy of LPA to manage patients with APAs; however, the 8% incidence of multifocal adenomas must be considered, especially in patients who remain hypertensive following surgery [20]. Also, patients who develop hypertension after a normotensive period must be screened for recurrence.

Pheochromocytoma

As with the surgical treatment of APAs, small adrenal pheochromocytoma management has shifted toward a laparoscopic approach; extra-adrenal pheochromocytomas are also increasingly managed in a similar manner [21,22]. The role of adrenal preservation is clear in patients with inheritable syndromes, such as MEN-2 and VHL, at risk for multiple adrenal tumors that are synchronous or metachronous. Partial adrenalectomy can preserve normal functioning adrenal tissue if adrenal-sparing surgery is not feasible in the contralateral adrenal gland [10]. Indeed, multiple reports document the value of open partial adrenalectomy for pheochromocytomas [7,23–26]. The laparoscopic approach for partial excision represents a logical extension of these goals and has been reported in the literature [27].

After the success of LPA for benign APAs, investigators [27–29] reported on the feasibility and efficacy of bilateral transperitoneal LPA for bilateral pheochromocytomas in adults and children. The efficacy of LPA in this setting was demonstrated, with no recurrences or requirements for long-term steroid supplementation. Other groups corroborated these early findings using LPA for pheochromocytomas [30,31].

LPA is of significant relevance for those with increased genetic risk of pheochromocytomas. Diner et al. [32••] reviewed the National Cancer Institute experience with 33 patients with hereditary pheochromocytomas who underwent 43 partial adrenalectomies (8 open, 25 laparoscopic). Ten patients underwent simultaneous bilateral partial adrenalectomy and eight underwent surgery on a solitary adrenal gland. The mean operating time for LPA was 215 minutes, with an estimated blood loss of 100 mL. Diner et al. [32••] used a 3-4 port technique before solely using an ultrasonic device (Harmonic Scalpel; Ethicon, Cincinnati, OH) instead of metal or plastic clips, electrocautery, or hemostatic sealants. Additionally, they routinely use intraoperative ultrasound to plan the resection. Interestingly, this modality detected additional lesions in three patients (8.5%) during LPA that were not visualized preoperatively on radiographic imaging studies.

In this study, five patients required postoperative steroid supplementation, including four of eight with solitary adrenal glands, and one of 10 who underwent bilateral LPA. On adrenocorticotropic hormone stimulation testing, these five patients who required supplementation had cortisol levels ranging from 1.9 to 15.1 μg/dL (normal 5–25 μg/dL). Four of these five patients were successfully weaned off steroids by 3 months postoperatively. At a mean follow-up of 36 months, all patients had normal serum and urinary catecholamine levels. However, local recurrence occurred in two patients with VHL after 36 and 52 months. These patients were subsequently managed with total adrenalectomy. Of interest, this group continues to manage nearly all nonhereditary sporadic pheochromocytomas and aldosteronomas with total adrenalectomy, secondary to the potentially higher risk of malignancy and microscopic multifocality in the former and latter, respectively [32••].

Bilateral pheochromocytomas can occur in up to 47% of affected patients, and contralateral lesions may develop in up to 60% of patients with MEN-2 and VHL. Partial adrenalectomy has evolved to balance tumor recurrence risk with lifetime risk of operative morbidity and long-term effects of steroid replacement after bilateral total adrenalectomy. The quality of life and medical risks associated with adrenal hypofunction are significant. Because these patients are at risk for contralateral tumor development, it seems logical to attempt to preserve adrenocortical function. LPA for pheochromocytomas yields outcomes similar to those with total adrenalectomy; largely due to reduced morbidity, minimally invasive LPA is a viable option in these patients [26,28,29,33].

Importantly, patients with inheritable syndromes are at risk for recurrent tumors in remnant adrenal tissue after partial adrenalectomy [28,34]. After open partial adrenalectomy, recurrent pheochromocytomas developed in the preserved remnant in 2 of 14 patients with pheochromocytomas due to VHL and MEN-2 [35]. After LPA, other series have shown that recurrent tumors developed in 15% to 20% of patients with VHL disease at a median of 18 to 40 months [26,33]; patients with MEN-2 have up to a 33% risk for recurrent pheochromocytoma at 54 to 88 months median follow-up [34]. Specific surveillance protocols after partial adrenalectomy have not been defined, but involve blood pressure measurement, plasma and urine catecholamines, and periodic imaging with CT, MRI, or metaiodobenzylguanidine (MIBG) scintigraphy, similar to surveillance after total adrenalectomy for pheochromocytoma. Although recurrences must be expected, they can often be managed with laparoscopy.

Surgical techniques

The most widely used laparoscopic approaches to the adrenal glands are transperitoneal or retroperitoneal. The transperitoneal approach is more familiar to surgeons; used for most laparoscopic renal surgery, it eases identification, dissection,

and mobilization of intra-abdominal structures. Potential disadvantages of the transperitoneal approach include ileus, adhesion formation, and injury to adjacent viscera.

The retroperitoneal approach provides the most direct route to the adrenal glands, and by not entering the abdominal cavity, may benefit those with extensive intra-abdominal adhesions. However, the working space is more confined and loss of easily identifiable landmarks may hinder the surgeon with limited experience using this approach. In terms of patient preparation, positioning, and trocar placement, LPA is similar to laparoscopic total adrenalectomy.

Laparoscopy offers a high degree of magnification and illumination. As discussed by Sasagawa et al. [14], tumors larger than 1.5 cm in diameter are easily distinguished from normal adrenal gland tissue. However, the exact location of tumor margins may not be clear. As surgeons increasingly use intraoperative ultrasound for laparoscopic partial nephrectomy, many embrace this modality during LPA [36,37]. Additionally, intraoperative ultrasound also has reported value during laparoscopic resection of extra-adrenal pheochromocytomas [38]. In these cases, ultrasonography identifies additional satellite lesions that are not evident on preoperative imaging, delineates the central adrenal vein, evaluates local invasion, and assesses the feasibility of partial resection if the mass is considerably large or is in a suboptimal location.

Because of the highly vascular nature of the adrenal gland, LPA poses a significant risk of bleeding. Many techniques for lesion excision, as well as adjunctive hemostatic measures, have been reported. The two most commonly used tools for lesion excision and hemostasis are electrocautery and ultrasonic energy. Many reports have confirmed the ultrasonic scalpel's efficacy in reducing bleeding when applied for partial adrenalectomy of adrenal adenomas or pheochromocytomas [13,14,31,33,39,40]. Additional measures to prevent delayed bleeding include use of argon beam coagulation, bipolar coagulation, fibrin glue, and clips [13,28].

The vascular stapler has also been used during LPA to excise lesions and provide hemostasis [39,41,42]. One concern with the stapling device is that it is not as precise as other methods of excision. Jeschke et al. [19] has abandoned using the device because it only allows a straight cut, and its diameter of 7 mm increases risk of removing excess tissue. Instead, electrocautery with endoscopic shears obtains a margin of normal tissue.

Other novel techniques have been reported. Liao et al. [43] examined their preliminary experience, performing 10 LPAs in eight patients using 2-mm working ports and needlescopic instruments. At mean follow-up of 25 months, seven patients experienced resolution of hypertension and one significantly reduced medication use. St. Julien et al. [44] recently reported the only published case of a robot-assisted cortical-sparing adrenalectomy in a patient with VHL disease who had previously undergone a total adrenalectomy for a pheochromocytoma 9 years earlier.

Although induction of anesthesia, surgical manipulation, pneumoperitoneum, and hypercapnia have been implicated as potential stimuli for catecholamine release and subsequent hypertensive crisis, laparoscopic resection has become a widely accepted approach for pheochromocytomas located in the adrenal gland [21,22]. When performing LPA for a pheochromocytoma, the surgeon must realize that this risk is theoretically increased because 1) there is a higher degree of gland manipulation during partial excision than in total extirpation, and 2) the adrenal vein is not routinely ligated in all LPA cases. However, current reports have not demonstrated this to be true, with no untoward risks of LPA specifically performed for pheochromocytoma. It is important to note that regardless of whether the surgical approach is open or laparoscopic, preoperative pharmacologic blockade and strict intraoperative hemodynamic management is of utmost importance during partial or total adrenalectomy. The patient should be properly prepared for surgery, with adequate hydration, α-adrenergic blockade, and β-adrenergic blockade to control arrhythmias.

Discussion

Despite growing interest and increasing reports on efficacy, partial adrenalectomy remains controversial. In 2006, Brunt [45] commented that LPA for unilateral tumors in patients who do not have an inherited predisposition to adrenal tumors represents a "departure from the established principles of adrenal surgery." He also suggested that contralateral adrenal loss is a rare event. In cases of APAs, nondominant nodules within the gland may be a source of aldosterone production. As a result, adrenal-sparing surgery should be considered only in highly selected patients.

Ishidoya et al. [46] published their experience with 92 patients diagnosed with primary hyperaldosteronism. This nonrandomized retrospective study compared unilateral total gland removal (n = 63) with partial adrenalectomy (n = 29). The median follow-up for the groups was 60.3 and 29.3 months, respectively. Indications for LPA were unilateral single adenoma associated with adequate abundance of normal adrenal tissue (n = 21) or bilateral disease (n = 5). Of LPAs, 23 were performed via a retroperitoneal approach and six via a transperitoneal approach. An ultrasonic device was used solely for hemostasis. No open conversions were reported and the LPA group had statistically shorter operative times, fewer number of ports, and equivalent blood loss. All 63 patients treated with total adrenal removal had resolution of hypertension and associated serum values. However, two of 29 patients who had LPA remained hypertensive with elevated plasma aldosterone levels. It was assumed that these patients must have had a functioning microadenoma in the preserved adrenal tissue. Additionally, pathologic examination of the 63 adrenal glands removed in their entirety revealed multiple microadenomas in 17 glands, possibly demonstrating APA multiplicity.

It is unclear whether these lesions represented aldosterone-secreting tissue or hyperplastic nodules, a question that immunostaining may elucidate. Further, Ishidoya et al. [46] reported that they did not find any clinical adverse effects such as postoperative hypotension or cortisol-related events in the group that had the entire adrenal removed. Although this is not a randomized study and corroborates that LPA is a feasible and safe procedure, the findings prompted a conclusion that total adrenal removal remains the more prudent option, except in cases of bilateral tumors or tumors in solitary glands. Similarly, although the benefit of adrenal preservation and LPA in patients with VHL or MEN-2 is clear, the utility of LPA in sporadic pheochromocytomas has not been defined.

LPA involves other concerns that have not been clearly addressed. One issue relates to the amount of adrenal tissue that must be preserved to avoid hormonal replacement therapy. Another issue involves the clinical difference between enucleation and partial adrenalectomy, if such a difference exists. Also, the ideal method of obtaining hemostasis has not been definitely achieved. Further, the question of central adrenal vein preservation remains unanswered. Clearly, some adrenal glands may function adequately despite ligation of the main vein [18]. Finally, no guidelines exist regarding acceptable indications for which adrenal masses are more suitable for treatment with an adrenal-sparing approach.

Conclusions

Minimally invasive surgery offers equivalent efficacy to traditional open procedures, while providing decreased postoperative pain, improved cosmesis, and shorter convalescence. Indeed, the laparoscopic approach has emerged as the standard extirpation in many surgical fields. Furthermore, surgeons have begun to use laparoscopy for complex reconstructive and organ-sparing surgeries, and investigators have proposed LPA to preserve adrenal tissue, forgoing the need for chronic steroid treatment and its associated sequelae. Current literature demonstrates that LPA is efficacious, safe, and represents a feasible intervention for select patients presenting with an aldosterone-producing adenoma or pheochromocytoma. More studies are required to answer questions related to the degree of adrenal-sparing required to provide adequate hormonal reserve, which technique is ideal for excision, and in what setting is the procedure indicated in terms of size, location, and relevant patient history. Aside from LPA, newer modalities such as cryosurgery and radiofrequency ablation have recently offered promising initial results, but further studies with longer follow-up are needed to address their efficacy and clinical utility.

Disclosures

No potential conflict of interest relevant to this article was reported.

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