Surgical Management of Adrenocortical Carcinoma

An Evidence-Based Approach

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KEYWORDS

• Adrenocortical carcinoma • Adrenalectomy • Surgery • Multimodality • Localized • Recurrence • Metastatic • Laparoscopic

KEY POINTS

- Adrenocortical carcinoma is an aggressive malignancy; prognosis is determined by tumor stage at presentation and completeness of surgical resection.
- Complete resection with negative margins is the goal of surgical management and may require multivisceral resection, tumor thrombectomy, or vascular resection with or without reconstruction.
- Extended resection including adjacent organs not obviously involved by tumor is not indicated. Regional lymphadenectomy may provide valuable staging information or be associated with a disease-free or overall survival advantage and is underutilized.
- Minimally invasive approaches have been advocated by select centers with expertise; notwithstanding, likely malignant and locally advanced lesions in particular are most safely managed with an open approach.
- Recurrence is associated with a poor prognosis; however, selected patients with limited or symptomatic disease may benefit from aggressive surgery.

INTRODUCTION

Adrenocortical carcinoma (ACC) is a rare malignancy with an annual incidence of 1 to 2 cases per million individuals.[1] Notwithstanding, frequent presentation with sequelae of steroid precursor overproduction, proclivity for aggressive local growth, early metastasis and recurrence, and the scarcity of effective systemic treatment options contribute to a substantial burden of disease. Women are more affected than men, at a ratio of 1.5:1. Although ACC affects individuals of all ages, cases are clustered

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in early childhood or middle age. Most cases are seemingly sporadic; however, ACC may arise in association with hereditary syndromes, including multiple endocrine neoplasia-1 and Li-Fraumeni syndrome.[2] Overall prognosis is poor; estimates of 5-year survival range from 30% to 50%; metastatic disease is associated with a median survival of less than 1 year.[3,4] Surgery is the cornerstone of therapy for localized disease and has a role in selected recurrent cases. Although an association between complete resection with negative margins and survival has been reproduced in numerous series, the frequent presentation with at least locally advanced disease and presence of major vascular invasion or direct invasion of discontiguous structures undermine effective surgical therapy in many cases. Moreover, presence of occult micrometastatic disease at the time of presentation is confirmed by frequent distant failure after apparent negative margin resection.[5] Owing in part to its low incidence, data for many accepted elements of therapy are limited or nonexistent. This review critically considers the existing evidence for elements of the evaluation and treatment of patients with ACC, with a particular focus on surgical management.

WHAT IS THE APPROPRIATE DIAGNOSTIC AND IMAGING WORKUP FOR PATIENTS WITH SUSPECTED ADRENOCORTICAL CARCINOMA?

The presentation of ACC is highly variable. Smaller nonfunctional ACCs are sometimes identified incidentally. Approximately 50% to 60% of ACCs are functional and present with signs or symptoms of hormone excess.[6] As with all tumors of the adrenal gland, directed laboratory testing and high-resolution imaging are critical and allow appropriate management. The former should include serum metanephrines to exclude pheochromocytoma. Glucocorticoid excess may be discerned through measurement of levels of serum cortisol and plasma adrenocorticotropic hormone or 24-hour free urinary cortisol; a more definitive diagnosis may require low-dose dexamethasone suppression. Levels of sex steroids and steroid precursors, including dehydroepiandrosterone sulfate (DHEA-S), 17-OH progesterone, androstenedione, testosterone, and 17-β-estradiol (in men and postmenopausal women), may be elevated in serum. Mineralocorticoid excess may be driven by glucocorticoid-mediated mineralocorticoid receptor activation in the occasional patient with hypercortisolism and is detected through measurement of the plasma aldosterone/renin ratio.[7,8] Urinary steroid metabolomic profiling has emerged as a promising diagnostic tool,[9] but it has yet to be validated in larger prospective multicenter series.

Computed tomography (CT) and MRI are similarly effective at discriminating between benign and malignant adrenal tumors and identifying metastases. The choice of one imaging study over another is largely a question of institutional preference with some caveats: (1) CT is less expensive and (2) MRI is preferable when pheochromocytoma is suspected because of the purported risk of a hypertensive crisis after intravenous infusion of iodinated CT contrast. Hounsfield units less than 10 on unenhanced CT, rapid washout at 15 minutes on delayed contrast-enhanced CT, or signal intensity loss using opposed-phase MRI are consistent with a benign tumor.[10,11] ACCs are typically heterogeneous with irregular margins and irregular enhancement of solid components (**Fig. 1**). With ACC, invasion of adjacent structures or extension into the inferior vena cava (IVC), locoregional lymph node metastases, and distant metastases may be seen. PET with fluorodeoxyglucose F^{18} may have additional sensitivity in identifying metastases.[12] Use of radiolabeled metomidate, highly specific for adrenal cortical cells via targeted binding to both 11β-hydroxylase and aldosterone synthase, for either PET- or single-photon emission CT–based functional imaging is another emerging technique with high sensitivity and specificity for ACC.[13]