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Outcomes after resection of cortisol-secreting adrenocortical carcinoma

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Abstract

BACKGROUND: We sought to define the impact of cortisol-secreting status on outcomes after surgical resection of adrenocortical carcinoma (ACC).

METHODS: The U.S ACC group database was queried to identify patients who underwent ACC resection between 1993 and 2014. The short-term and long-term outcomes were assessed.

The authors declare no conflicts of interest.

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RESULTS: The incidence of all functional and cortisol-secreting tumors was 40.6% and 22.6%, respectively. On multivariable analysis, cortisol secretion remained associated with an increased risk of postoperative complications (odds ratio = 2.25, 95 % confidence interval = 1.04 to 4.88; $P = .04$). At a median follow-up of 17.6 months, 118 patients (50.4%) had developed a recurrence. On multivariable analysis, after adjusting for patient and disease-related factors cortisol secretion independently predicted shorter recurrence-free survival (Hazard ratio = 2.05, 95% confidence interval = 1.16 to 3.60; $P = .01$).

CONCLUSIONS: Cortisol secretion was associated with an increased risk of postoperative morbidity. Recurrence remains high among patients with ACC after surgery; cortisol secretion was independently associated with a shorter recurrence-free survival. Tailoring postoperative surveillance of ACC patients based on their cortisol secreting status may be important.

Although adrenocortical carcinoma (ACC) is often diagnosed as an incidental finding on cross-sectional imaging, up to 40% to 60% of patients present with symptoms.[1] Clinical syndromes are typically secondary to the autonomous production of hormones that include androgens, estrogens, mineralocorticoids, and corticosteroids.[2,3] Unlike patients with nonfunctional tumors who may present with nonspecific symptoms related to local mass effects of the tumor such as abdominal pain,[4,5] patients with functional tumors often present with very hormone-specific symptoms. For example, androgen-secreting tumors can lead to gynecomastia and testicular atrophy,[6] whereas excessive mineralocorticoid secretion commonly induces hypertension.[7] In addition, cortisol-secreting tumors commonly present with rapidly progressing Cushing's syndrome.[8,9]

Cortisol-secreting tumors are the most common hormonal-functional ACCs.[3] However, the impact of cortisol-secreting tumors and their distinct biologic behavior remain poorly defined. Cortisol has been demonstrated in general to suppress immune surveillance by blunting the cellular immune response possibly leading to tumor growth and recurrence.[10] Of note, recurrence after ACC surgery is particularly common, occurring in 50% to 90% of patients.[6,11–13] To date, only a handful of single-institution studies have explicitly examined the effect of cortisol-secretion on the long-term outcomes of patients with ACC.[14–17] More importantly, these studies have suffered from small sample size, conflicting results, and variable inclusion criteria.[14–17] As such, the objective of the present study was to examine the outcomes of patients with cortisol-secreting ACC tumors using a large, multicenter collaborative database. In particular, given that cortisol-secreting ACC tumors are the most common hormonal tumor, and the importance of determining prognosis after surgical management of ACC, we sought to define the short-term outcomes and the long-term prognostic impact of cortisol secretion among patients who underwent resection of ACC.

Methods

Study design

Patients were identified from a retrospective, multi-institutional database of 234 patients who underwent surgery for ACC between 1993 and 2014 at 13 major cancer centers in the United States. The 13 institutions participating in the study included Johns Hopkins Hospital, Baltimore, MD; Emory University, Atlanta GA; Stanford University, Palo Alto, CA; Washington University, St. Louis, MO; Wake Forest University, Winston-Salem, NC; University of Wisconsin, Madison, WI; The Ohio State University, Columbus, OH; Medical College of Wisconsin, Milwaukee, WI; New York University, New York, NY; University of California at San Diego, San Diego, CA; University of California at San Francisco, San Francisco, CA; University of Texas Southwestern Medical Center, Dallas, TX; and Vanderbilt University Medical Center, Nashville, TN. Only patients with histologically confirmed ACC were included in the study group. Overall, patients less than 18 years old were excluded in the present study. The Institutional Review Board of each institution approved the study.

Data on patient demographic and clinicopathologic features including age, sex, race, and tumor-specific characteristics were collected. In particular, data were obtained on ACC tumor size, weight, laterality, lymph node status, and presence of capsular invasion. In addition, we recorded the presence of clinical signs and symptoms. Data on T stage were also collected according to 7th edition American Joint Committee on Cancer staging system.[18] Resection margin status was recorded and classified as microscopically negative (R0), microscopically positive (R1), or macroscopically positive (R2). Mitotic rate was defined as number of mitoses/50 high-powered field (HPF). Definition of the functional status of ACC was based on the standard biochemical evaluation of hormone excess. Patients with elevated hormone levels were considered to be hyper secreting irrespective of the presence of clinical symptoms. Furthermore, data regarding treatment details of ACC were collected, including surgical approach and receipt of adjuvant chemotherapy and mitotane. Perioperative complications and mortality were considered within 30 days from the operation. Complications were categorized based on the Clavien-Dindo classification system, with minor complications defined as grade I or II and major complications as grade III or IV.[19] Additional data on the occurrence of postoperative adrenal insufficiency were collected. In addition, the length of hospital stay, date of