ESE Clinical Guideline Summary

European Society of Endocrinology Clinical Practice Guidelines on the Management of Adrenocortical Carcinoma in Collaboration with the European Neuroendocrine Tumours Society

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Introduction

Adrenocortical carcinoma (ACC) is a rare cancer with an annual incidence of about 1 per one million, translating to ~750 cases per year in Europe.

About 50-60% of these patients present with autonomous adrenal hormone excess (mostly Cushing's syndrome, androgen excess or a mixture) and 30-40% complain of pain or abdominal discomfort due to the abdominal mass (average size of the tumor is about 11 cm).

In an increasing number of cases (10-15%) ACC is an incidental finding on imaging. In general, clinical outcome is poor with a median overall survival of about 3-4 years. However, prognosis is variable (even within a given tumor stage).

Here, we shortly summarise the first international guidelines that are based on a systematic review of the available literature. It was initiated by the European Society of Endocrinology and co-sponsored by the European Network for the Study of Adrenal Tumors (ENSAT) and published in summer 2018 in the European Journal of Endocrinology.

Guideline Aims

The purpose of these guidelines is to provide clinicians with best possible evidence-based and expert recommendations for clinical management of patients with ACC based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system.

We predefined four main clinical questions, which were judged as particularly important for the management of ACC patients and performed systematic literature searches:

A. What is needed to diagnose an ACC by histopathology?

B. Which are the best prognostic markers in ACC?

C. Is adjuvant therapy able to prevent recurrent disease or reduce mortality after radical resection?

D. What is the best treatment option for macroscopically incompletely resected, recurrent or metastatic disease?

Selected Recommendations

i. We recommend that all patients with suspected and proven ACC are discussed in a multidisciplinary expert team meeting

ii. We recommend that every patient with (suspected) ACC should undergo careful clinical assessment, detailed endocrine work-up to identify autonomous hormone excess, and comprehensive imaging with focus on the adrenal, but also on potential metastases.

iii. We recommend that adrenal surgery for (suspected) ACC should be performed only by surgeons experienced in adrenal and oncological surgery aiming at a complete en-bloc resection (including resection of oligo-metastatic disease).

iv. We suggest that all suspected ACC should be reviewed by an expert adrenal pathologist using the Weiss score and providing the exact value of Ki67 index.

v. We suggest adjuvant mitotane treatment in patients after radical surgery that have a perceived high risk of recurrence (ENSAT stage III, or R1 resection, or Ki67 >10%).

vi. For advanced ACC not amenable to complete surgical resection, local therapeutic measures (e.g. radiation therapy, radiofrequency ablation, chemo-embolization) are very helpful options. However, we suggest against the routine use of adrenal surgery in case of widespread metastatic disease. In these patients we recommend either mitotane monotherapy or mitotane, etoposide, doxorubicin, and cisplatin depending on prognostic parameters. In case of severe Cushing syndrome agents inhibiting steroidogenesis can be safely administered in association to EDP plus mitotane with the aim to attain a rapid control of hypercortisolism. In selected patients with a good response, surgery may be subsequently considered.

vii. In patients with recurrent disease and a disease-free interval of at least 12 months, in whom a complete resection/ablation seems feasible, we recommend surgery or alternatively other local therapies.

Furthermore, we offer detailed recommendations about the management of mitotane treatment and other supportive therapies. Finally, we suggest directions for future research.

The full guidelines are available online at: https://doi.org/10.1530/EJE-18-0608