Treatment of Cushing's Syndrome

Surgical and medical management, remission assessment, and long-term monitoring for confirmed Cushing's syndrome.

2015 Endocrine Society
Treatment of Cushing's Syndrome Guideline
Nieman et al. · JCEM 2015;100:2807–2831

GRADE · 1 · Strong · 2 · Suggest For · 2- · Suggest Against · Ungraded / Best Practice

1 Treatment Goals & Adjunctive Care

1 **Normalize cortisol/action** to eliminate signs/symptoms and treat comorbidities in overt CS. **Against** treating without an established diagnosis, or normalizing cortisol for borderline HPA abnormality without specific CS signs.

GPS Provide **patient/family education**; monitor and treat **cortisol-dependent comorbidities** (psychiatric, diabetes, hypertension, hypokalemia, infection, dyslipidemia, osteoporosis, fitness) in all patients; use a **multidisciplinary team**; offer age-appropriate **vaccinations** (flu, zoster, pneumococcal).

2 Evaluate **VTE risk factors**; provide **perioperative VTE prophylaxis** for surgical patients.

2 First-Line Surgical Treatment

ETIOLOGY	APPROACH
Cushing's disease (pituitary)	Transsphenoidal selective adenomectomy (TSS) by an experienced surgeon (1) — check serum Na days 5–14 postop, free T4/prolactin at 1–2wk, pituitary MRI at 1–3mo
Ectopic ACTH tumor	Localize and resect, with node dissection as appropriate (1)
Unilateral adrenal disease	Unilateral adrenalectomy by an experienced adrenal surgeon (1)
Bilateral adrenal disease	Surgical resection (1); for BMAH, medical therapy to block aberrant hormone receptors is an option (2)

3 Remission & GC Replacement

GPS **Individualize** postop management by cortisol status (hypo-, hyper-, or eucortisolism). Treat **persistent overt hypercortisolism** further (1); measure late-night salivary/serum cortisol if eucortisolism after TSS (1); screen for **recurrence** in ACTH-dependent CS (1).

1 **Glucocorticoid replacement** + adrenal insufficiency education for hypocortisolemic patients after surgical remission. Follow-up AM cortisol and/or ACTH-stimulation/insulin-tolerance test to assess HPA recovery; discontinue GC once normal. Reassess other pituitary axes postop.

4 Second-Line Options

OPTION	USE CASE
Shared decision-making	Noncurative surgery or inoperable ACTH-dependent CS — choose among repeat TSS, radiotherapy, medical therapy, bilateral adrenalectomy (2)
Bilateral adrenalectomy	Occult/metastatic ectopic ACTH secretion, or life-preserving emergency for uncontrolled disease (2); monitor for corticotrope tumor progression (MRI + ACTH) afterward (1)
Repeat TSS	Incomplete resection or residual pituitary lesion on imaging (2)
Radiotherapy/radiosurgery	Confirm medical therapy controls cortisol first (1); use after failed TSS/recurrent CD (2), or for mass effect/invasion concerns (1); monitor cortisol/UFC off-medication q6–12mo (1)
Medical therapy (steroidogenesis inhibitors)	Second-line after TSS ± RT; primary therapy for ectopic ACTH secretion or ACC when surgery isn't an option

5 Long-Term Monitoring & Special Populations

1 **Lifelong comorbidity monitoring** + recurrence testing (except after adrenal adenoma resection with CT density <10 HU). Educate on features of remission (GPS). Adrenal adenoma follow-up per CT density (2); Carney complex — lifelong cardiac myxoma and associated-disease surveillance (1).

1 **Urgent treatment (within 24–72h)** of hypercortisolism if life-threatening complications are present — infection, pulmonary thromboembolism, cardiovascular complications, or acute psychosis — while addressing the associated disorder.

Nieman LK, Biller BM, Findling JW, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2015;100(8):2807–2831.