Cushing's disease prognosis

- Weight gain reversibility and BMI following treatment for Cushing's syndrome: long-term outcomes and potential predictors
- Postoperative Initiation of Thromboprophylaxis in patients with Cushing's Disease (PIT-CD): a randomized controlled trial
- Specific focus on the basal dura for improving Cushing's disease surgery: a cohort study
- PANOMEN-3 grading score is reliable in predicting pituitary adenoma behavior and prognosis: a single center cohort study
- Survival probabilities in patients with ectopic Cushing's syndrome-a systematic review and a single-arm meta-analysis
- Matching-Adjusted Indirect Comparison of Osilodrostat Versus Metyrapone for the Treatment of Cushing's Syndrome
- Clinical Implications of Molecular and Genetic Biomarkers in Cushing's Disease: A Literature Review
- Long-Term Response of Equids With Pituitary Pars Intermedia Dysfunction to Treatment With Pergolide

Cushing's disease is caused by an adrenocorticotropic hormone (ACTH)-secreting pituitary adenoma, leading to hypercortisolism. The prognosis of Cushing's disease depends on several factors, including the timeliness of diagnosis, the success of treatment, and the presence of complications related to prolonged hypercortisolism.

Factors Influencing Prognosis

1. **Timely Diagnosis and Treatment** Early detection and treatment significantly improve outcomes by reducing the risk of complications associated with prolonged exposure to excess cortisol.

2. Surgical Outcomes

- 1. **Transsphenoidal surgery**, the standard treatment, is highly effective when performed by experienced neurosurgeons, with remission rates of 70–90% for microadenomas and lower success rates for larger or invasive macroadenomas.
- 2. Recurrence rates after surgery range from 10–30%, typically within the first five years postsurgery.

3. **Residual or Recurrent Disease** Patients with incomplete tumor resection or recurrence may require additional interventions such as repeat surgery, radiation therapy, or medical management.

4. **Adrenal Function Recovery** Successful treatment often results in secondary adrenal insufficiency, necessitating temporary or long-term glucocorticoid replacement therapy. The duration of this recovery can vary.

- 5. **Complications of Hypercortisolism** Prolonged exposure to high cortisol levels can result in:
 - 1. Cardiovascular diseases (e.g., hypertension, atherosclerosis)
 - 2. Diabetes mellitus
 - 3. Osteoporosis
 - 4. Muscle weakness

- 5. Psychiatric disorders (e.g., depression, anxiety)
- 6. Impaired immune function

These complications may not fully resolve even after remission, impacting long-term health.

6. **Mortality Risk** Untreated or persistent Cushing's disease is associated with a significantly increased mortality risk, primarily due to cardiovascular and metabolic complications. Remission can reduce this risk, bringing mortality rates closer to those of the general population.

7. **Quality of Life** Many patients experience an improvement in quality of life after remission, but residual physical and psychological effects (e.g., fatigue, depression) can persist, necessitating ongoing management and support.

Long-term Monitoring Long-term follow-up is essential to monitor for recurrence and manage any residual effects of hypercortisolism. This includes: - Periodic biochemical testing (e.g., 24-hour urinary free cortisol, late-night salivary cortisol) - Imaging studies if clinically indicated - Addressing cardiovascular and metabolic risks

Summary - The prognosis of Cushing's disease is generally favorable if treated early and effectively. - Long-term outcomes depend on the success of initial treatment and management of complications. - Regular follow-up is critical to monitor for recurrence and manage residual health issues.

Untreated, diabetes mellitus and hypertension can occur in Pituitary corticotroph adenoma and increase the patient's morbidity and mortality. Early recognition and appropriate referral can reverse the signs and symptoms over time and lead to a significantly improved quality of life.

Patients diagnosed with CD after 45 years of age have a significantly lower survival probability than other PA subtypes in the first 15 years of follow-up. All other PA subtypes had a similar survival probability after adjusting for age and sex. Due to advances in medical treatment of hormone secreting tumors, mortality in patients with PAs might increasingly depend more on tumor mass than on hormonal hypersecretion ¹⁾.

Cushing's disease (CD) is associated with an increased risk of venous thromboembolism. The purpose of the review was to discuss preventive strategies for post-operative thrombosis in CD patients and their impact on patient outcomes. A systematic review under PRISMA guidelines was conducted within PubMed, Embase, Web of Science, and Cochrane databases through July 2022. Of the 3207 papers retrieved, seven articles were included in a systematic review. Four hundred forty-eight patients were presented in the reviewed studies and the overall reported mortality was 2.67% (12/448). Three studies utilized prophylaxis methods including graduated compression stockings (GCS) and early ambulation (EA) while the remaining four studies only used anticoagulation medicine. Only 20 patients received pre-operative prophylactic treatment, while 366 patients received post-operative prophylaxis which was delivered either immediately after surgery or at different time intervals within 2 days following the surgery. Thrombotic events mainly occurred within two to 3 months after surgery. Overall, a higher frequency of thromboembolic events and mortality was observed in the control groups in comparison to groups receiving prophylaxis. A combination of anticoagulation, EA,

and GCS might reduce thrombotic events and mortality in CD patients after treatment. Although the early commencement of a prophylactic anticoagulation regimen on the same day of surgery and continuing up to 3 months seems beneficial, the application of a prophylactic regimen should be utilized with caution since the number of included studies was insufficient to draw a strong conclusion, as well as neither prospective study nor randomized controlled trials existed ²⁾.

After remission of Cushing's disease (CD), TSH, T3, and Free T3 increased significantly, even above the reference range, but returned to normal one year after surgery in most cases. Antithyroid antibodies didn't change significantly after remission of CD³.

Pituitary corticotroph adenoma recurrence

Pituitary corticotroph adenoma recurrence.

Multicenter retrospective cohort studies

Despite growing interest in how patient frailty affects outcomes (eg, in neuro-oncology), its role after transsphenoidal surgery for Cushing disease (CD) remains unclear. They evaluated the effect of frailty on Cushing's disease prognosis using the Registry of Adenomas of the Pituitary and Related Disorders (RAPID) data set from a collaboration of US academic pituitary centers.

Data on consecutive surgically treated patients with CD (2011-2023) were compiled using the 11factor modified frailty index. Patients were classified as fit (score, 0-1), managing well (score, 2-3), and mildly frail (score, 4-5). Univariable and multivariable analyses were conducted to examine outcomes.

Data were analyzed for 318 patients (193 fit, 113 managing well, 12 mildly frail). Compared with fit and managing well patients, mildly frail patients were older (mean \pm SD 39.7 \pm 14.2 and 48.9 \pm 12.2 vs 49.4 \pm 8.9 years, P < .001) but did not different by sex, race, and other factors. They had significantly longer hospitalizations (3.7 \pm 2.0 and 4.5 \pm 3.5 vs 5.3 \pm 3.5 days, P = .02), even after multivariable analysis (β = 1.01, P = .007) adjusted for known predictors of prolonged hospitalization (age, Knosp grade, surgeon experience, American Society of Anesthesiologists grade, complications, frailty). Patients with mild frailty were more commonly discharged to skilled nursing facilities (0.5% [1/192] and 4.5% [5/112] vs 25% [3/12], P < .001). Most patients underwent gross total resection (84.4% [163/193] and 79.6% [90/113] vs 83% [10/12]). No difference in overall complications was observed; however, venous thromboembolism was more common in mildly frail (8%, 1/12) than in fit (0.5%, 1/193) and managing well (2.7%, 3/113) patients (P = .04). No difference was found in 90-day readmission rates.

These results demonstrate that mild frailty predicts CD surgical outcomes and may inform preoperative risk stratification. Frailty-influenced outcomes other than age and tumor characteristics may be useful for prognostication. Future studies can help identify strategies to reduce the disease burden for frail patients with hypercortisolemia⁴⁾.

This study highlights the importance of frailty in predicting outcomes after transsphenoidal surgery for CD, offering a foundation for integrating frailty into preoperative assessments. However, the small sample size of mildly frail patients, retrospective design, and lack of long-term outcomes temper the strength of the conclusions. Further research is needed to validate these findings and explore interventions to mitigate the impact of frailty on surgical outcomes in CD.

1)

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