CUSHING’S DISEASE
Morbidity and Mortality

ROLE OF HYPERCORTISOLISM IN CUSHING’S DISEASE

If only symptoms of Cushing’s disease are treated, the underlying cortisol overproduction remains unaffected.

INCREASED RISKS FOR PATIENTS WITH CUSHING’S DISEASE

A population-based cohort study found that Cushing’s syndrome is associated with increased mortality and multisystem morbidity, even before diagnosis and treatment.*

This study measured the hazard ratio (HR) of several serious health risks, denoting the probability of the event occurring among the Cushing’s disease population as a ratio compared to the control cohort population. Hazard ratios were obtained with a 95% confidence interval (CI).

CARDIOVASCULAR EVENTS:

- Stroke: 2x HR
- Acute myocardial infarction (AMI): 3.7x HR
- Venous thromboembolism (VTE): 2.6x HR
- Peptic ulcers: 2x HR
- Infections: 4.9x HR
- Fractures: 1.4x HR

EFFECT OF EXPOSURE TO HYPERCORTISOLISM OVER TIME

The longer the exposure to excess levels of cortisol, the higher the mortality rate and the more difficult it becomes to reverse complications associated with Cushing’s disease.

*Based on a population-based cohort study.
IMPACT OF MONITORING CORTISOL LEVELS

Remission in Cushing’s disease is assessed by immediate post-surgical measurement of serum cortisol levels.

Criteria for post-surgical remission

<table>
<thead>
<tr>
<th>Serum cortisol levels*</th>
<th>Remission status</th>
<th>Urinary free cortisol levels‡</th>
<th>Remission status</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 µg/dL</td>
<td>Remission and a recurrence rate of -10% at 10 years</td>
<td>&lt;20 µg/24h</td>
<td>Suggests remission</td>
</tr>
<tr>
<td>&lt;5 µg/dL†</td>
<td>Further evaluation required</td>
<td>Normal range (20-100 µg/24h)</td>
<td>Ambiguous</td>
</tr>
<tr>
<td>&lt;2 µg/dL</td>
<td>Considered in remission</td>
<td>Above normal range</td>
<td>Persistent tumor</td>
</tr>
</tbody>
</table>

Post-surgical remission is not always long lasting and therefore, long-term follow-up with regular monitoring of cortisol levels are critical.

*Post-operative, early morning; † for up to 6 weeks following surgery; ‡ evaluation can be useful if serum cortisol levels are ambiguous

IMPORTANCE OF LONG-TERM FOLLOW-UP

Among Cushing’s disease patients who achieve remission, the mortality rate is reduced to that observed in the general population.

Normalizing cortisol levels can effectively:

- Reduce cardiovascular risk factors
- Partially reverse cognitive decline
- Partially reverse bone damage

Timely diagnosis and intervention, along with ongoing monitoring of cortisol levels, are critical to reducing multiple morbidities and can lead to the normalization of mortality rates. To learn more, visit www.CushingsDisease.com within the US and www.AboutCushings.com outside of the US.

*Based on “Multisystem Morbidity and Mortality in Cushing’s Syndrome: A Cohort Study” by Dekkers, O., et al., published in Journal of Clinical Endocrinology Metabolism in June 2013