**Serum cortisol response to transsphenoidal surgery for Cushing disease**

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Object. Transsphenoidal surgery remains the optimal treatment for Cushing disease, but the definitions of surgical cure and failure remain debatable. In this study the authors evaluated serum cortisol levels in patients before and after they underwent transsphenoidal surgery to elucidate the patterns of cortisol decrease and the optimal time and criteria for determining surgically induced remission.

Methods. Twenty-seven patients were evaluated throughout an 8-month period. Serum cortisol levels were obtained before surgery and at 6-hour intervals postoperatively. No exogenous steroid medications were administered until after cortisol sampling was discontinued, following diagnosis of remission.

Twenty-one (78%) of 27 cases were labeled initial surgically induced remissions. Twenty-two (81%) of 27 cases were deemed surgically induced remissions at follow-up examination. Following surgery, initial remissions and failures demonstrated divergent patterns of cortisol levels. No patient whose condition was deemed an initial surgically induced remission has experienced definitive relapse of disease since discharge. One patient whose condition was initially deemed a surgical failure, eventually was found to exhibit surgically induced remission without further intervention.

Conclusions. Given such findings, exogenous steroid medications do not appear to be required for patients until after the determination of remission. During the 1st postoperative day, there is a time period during which serum cortisol values significantly differ between the categories of surgically induced remissions and surgical failures. Surgically induced remissions were identified when postoperative values of cortisol were lower than preoperative midnight levels and when absolute values of cortisol were less than 10 μg/dl. In a small proportion of patients remission on a delayed basis may also be demonstrated. These data allow for a simple and rapid determination of postoperative remission in patients undergoing transsphenoidal surgery for Cushing disease.

**KEY WORDS** • Cushing disease • hypercortisolism • transsphenoidal approach • pituitary adenoma

Pituitary adenomas represent one of the most common tumors encountered by the practicing neurosurgeon, with some estimates reaching as high as 14 new cases each year per 100,000 individuals. Pituitary dependent ACTH-secreting tumors, such as those that occur in Cushing disease, account for approximately 14% of such adenomas. The treatment of Cushing disease has included bilateral adrenalectomy, radical hypophysectomy, pituitary irradiation, and selective transsphenoidal microadenomectomy. Selective adenomectomy has evolved into the treatment of choice for most patients, with this method affording a timely cure, minimal risk of morbidity, and retention of an intact hypothalamic–pituitary axis postoperatively.

Surgical success rates in patients with Cushing disease vary throughout the literature, ranging from 52 to 89%. Reported recurrence rates in patients with these adenomas also demonstrate significant variability, ranging from 5 to 15%. Not only do second operations tend toward less chance of successful outcome (35–73%), but they also portend moderately increased complication rates. The decreased surgical efficacy in recurrent and persistent Cushing disease emphasizes the value of adequate initial treatment for these patients. Because of the inherent risks of morbidity and mortality associated with hypercortisolism, patients with persistent Cushing disease following transsphenoidal surgery require swift and efficient identification to be considered for additional therapy.

The abundance of reports detailing surgical success rates is sharply contrasted by the lack of an accepted definition of disease remission. Different centers adhere to differing standards by which they classify cases as surgically induced remissions or surgical failures. Qualitative attempts to determine outcome have included identification of tumor on imaging studies, visualization of the adenoma during resection, confirmed adenoma resection by pathological analysis, and/or clinical resolution of symptoms following surgery. Laboratory investigations have included static and temporal measurements of serum ACTH and cortisol, urinary free cortisol levels,
and serum cortisol responses to low- and high-dose dexamethasone suppression tests. This enormous variability in criteria severely limits the comparison of outcome rates within the literature. Ultimately, though, the definition for a given remission must document the removal of an ACTH-producing adenoma by either demonstrating resumption of the patient’s normal endogenous hypothalamic–pituitary axis function or the absence of sufficient endogenous cortisol production. The precise timing and method of sampling to achieve this goal remains elusive.

Central to these debates is the understanding of interactions among corticotropin-releasing factor, ACTH, and cortisol both in the presence of Cushing disease and following the removal of the ACTH-producing adenoma. Hypersecretion of ACTH by a tumor likely supresses, to varying degrees, the endogenous release of corticotropin-releasing factor and ACTH through feedback inhibition. Fearing complete suppression of the hypothalamic–pituitary axis, many neurosurgeons administer exogenous stress-dose steroid agents to patients with Cushing disease undergoing transsphenoidal surgery to avert adrenal insufficiency. This practice often delays the determination of remission due to the fact that serum and urine samples cannot be obtained until after the immediate and early postoperative periods because of the presence of exogenous steroids, which may erroneously elevate measurements in standard assays or suppress endogenous cortisol secretion.

To establish quantitative criteria by which to determine surgically induced remission, we believe that an expanded knowledge of postoperative cortisol dynamics was necessary. Twenty-seven patients with confirmed Cushing disease underwent serial measurements of serum cortisol sampled throughout the immediate and early postoperative periods. A review of these patterns allowed insight into the fluctuation of cortisol levels and elicited suggestions regarding a system of sampling for defining surgically induced remission.

Clinical Material and Methods

Patient Population

The patient population consisted of 27 patients (25 females and two males) whose ages ranged from 10 to 59 years (mean 37.8 years). In all patients the diagnosis of Cushing disease was determined using standard endocrinological methods; it was based on elevated urine free cortisol and serum cortisol levels, as well as cortisol suppression after high-dose dexamethasone testing conducted following failure of suppression after a low-dose dexamethasone challenge. Tumors were visible on preoperative imaging studies in 24 (89%) of 27 patients. No preoperative or intraoperative exogenous steroid medications were administered. In all patients selective transphenoidal microadenomectomy was performed at the University of Virginia Health Sciences Center by the senior author (E.R.L.). The operations commenced between 7:30 a.m. and 10:00 a.m.

Serum cortisol measurements were prospectively obtained by sampling through an indwelling heparin lock cannula inserted in a forearm vein. Samples were prepared using a cortisol kit (Immuilite cortisol kit; Diagnostic Products Corp., Los Angeles, CA) and measured by an immunoassay analyzer (Immuilite automated immunoassay analyzer; Diagnostic Products Corp.). Turnaround time was generally less than 2 hours (20 minutes after insertion into the analyzer), and this method offered a minimal detection of 1 μg/dl. In the event that some diurnal variation remained in these patients, preoperative samples were obtained in every case at midnight before surgery to measure the patient’s lowest endogenous cortisol level prior to surgery. Postoperative levels were obtained at 6:00 p.m. on the day of surgery and every 6 hours thereafter until disease remission was determined or the patient was discharged from the hospital. Samples were obtained at fixed points throughout the day, as opposed to individually set times following surgery, for several reasons. First, sampling was found to be more organized and less prone to error if the samples were obtained at regular points throughout the day. We believe this would hold true at most institutions. Equally important is the concern for the resumption of circadian cortisol secretion postoperatively, which mandates that samples be obtained in patients at similar times so that daily variations do not confuse the data. No exogenous steroids were administered during the sampling period. In patients in whom repeatedly low serum cortisol measurements were exhibited (< 10 μg/dl, as determined postoperatively), as well as clinical signs of adrenal insufficiency, disease remission was presumed to have been achieved, and exogenous steroids were administered. Four patients were removed from the study following the measurement obtained at 6:00 a.m. on postoperative Day 1 and six additional patients were removed from the study after sampling at noon on postoperative Day 1 because of the determination of initial remission reflected by low cortisol levels and symptoms of steroid withdrawal.

The patients in this study were followed for signs of relapse or adrenal insufficiency for 18 to 34 months (mean 27 months). Based on the clinical and laboratory findings obtained during return visits, patients were stratified into surgically induced remission or surgical failure groups. Surgically induced remissions are defined in this paper as those cases in which patients underwent transsphenoidal surgery and eventually were endocrinologically proven to have no evidence of hypercortisolism at distant postoperative evaluation. Follow-up testing included assessment of 24-hour urinary free cortisol and plasma cortisol and was generally performed at intervals of 1 to 3 months after discharge. The term “surgical failure” is used to indicate those cases in which patients exhibited persistent hypercortisolism at outpatient follow-up examination. Patients were prospectively placed into initial or early remission or failure groups based on their serum cortisol measurements and clinical symptoms during the immediate postoperative period (serum cortisol level < preoperative value and < 10 μg/dl, and symptoms of steroid withdrawal during postoperative Day 1). The reliability of the prospective analysis was assessed by the endocrinological follow-up examinations as described previously.

Statistical Analysis

Statistical analysis was performed using a commercially available software program (Statistica for Windows, version 5.1; StatSoft, Inc., Tulsa, OK). Analysis of vari-

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Results

Twenty-four of the 27 cases with microadenomas were diagnosed on the basis of findings on preoperative magnetic resonance imaging. Following selective transsphenoidal microadenomectomy, pathological evaluation revealed tumor with immunocytochemical positivity for ACTH in all but one specimen. Twenty-one (78%) of 27 patients were assigned to the initial surgically induced remission group following evaluation. Surgically induced remission was confirmed in all 21 patients at follow-up examinations. All but one patient assigned to the initial surgical failure group demonstrated persistent hypercortisolism at return visits. The remaining patient was assigned to the initial surgical failure group, but remission of disease was ultimately determined at an 8-month return visit, prompting the patient’s reassignment to the late surgically induced remission group.

Figure 1 shows the temporal pattern of serum cortisol values in all patients. Preoperative midnight cortisol levels ranged from 11 to 29 μg/dl (mean 19.6 ± 5 μg/dl). No statistical difference in mean preoperative cortisol levels was noted between the two groups (surgically induced remission group 19.36 ± 5.5 μg/dl; surgical failure group 17.6 ± 4.72 μg/dl). Following the operation, in 18 patients (14 of the 22 patients eventually assigned to the surgically induced remission group and four of the five patients eventually assigned to the surgical failure group) the first measured postoperative serum cortisol levels were elevated in comparison to preoperative levels. Cortisol levels measured at midnight on postoperative Day 1, however, were noted to have decreased from immediately postoperative levels in 20 of the 21 patients assigned to the initial surgically induced remission group. This trend occurred in only two of six patients assigned to the surgical failure group.
The average serum cortisol value was calculated with respect to the surgically induced remission and surgical failure groups. The analysis included averages of absolute serum cortisol values found in each group (Fig. 2). Significant differences between groups can be seen at multiple points throughout the postoperative period.

To evaluate surgically induced remission, postoperative cortisol levels were stratified according to preoperative value. Patients were stratified into one of two groups by defining the postoperative cortisol level to be either less than or equal to the preoperative midnight level, or greater than the preoperative midnight level. Table 1 shows the percentage of patients in whom postoperative cortisol levels were lower than preoperative midnight values at each measured interval. Data obtained in univariate logistic regression analysis of prediction of remission with respect to whether a certain postoperative cortisol value was higher than the preoperative value as well as the sensitivity, specificity, predictive value positive, and predictive value negative for each variable are shown in Table 2.

Discussion

In patients with Cushing disease, eliminating the hypercortisolism is paramount to reduce the morbidity and mortality of the condition. The widely accepted initial treatment for these patients is transphenoidal microadenocytom. Unfortunately, in a small but substantial percentage of patients who undergo attempted resection of an ACTH-secreting pituitary adenoma the initial operative therapy will fail. Identification of these patients is vital so that appropriate further therapy might be initiated. Multiple studies have attempted to define parameters by which to identify surgical failures; however, there continues to be significant disparity among reports. Established practice at the University of Virginia Health Sciences Center has maintained the routine of withholding perioperative exogenous steroid medications from patients undergoing transphenoidal surgery for Cushing disease. Given such a setting, it was believed that an investigation of these patients could allow for an improved understanding of cortisol dynamics and, possibly, clarify the debate of when and how to define remission following surgery.

The results of this study offer insight into the treatment of Cushing disease with particular emphasis on the fluctuating nature of cortisol following surgery and, based on such data, how early remission might be accurately assessed. Personnel at most centers routinely administer perioperative (both pre- and postoperative) exogenous stress-dose steroid agents, despite the inherent hypercortisolemic state of these patients.2,11,14,18,19,22–24 Other practitioners selectively administer steroids during the postoperative period.1 The rationale for administering exogenous steroids assumes that the excess cortisol inherent in the diseased state has completely suppressed the endogenous hypothalamic–pituitary axis. During periods of physiological stress, the normal response of increased steroid production would therefore be absent.11 In this study, without exogenous steroids, the initial postoperative cortisol level
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TABLE 1
Percentages of patients with postoperative cortisol levels lower than preoperative midnight values

<table>
<thead>
<tr>
<th>Group</th>
<th>POD0 (%)</th>
<th>POD1 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Midnight</td>
<td>6 a.m.</td>
</tr>
<tr>
<td>surgically induced remission</td>
<td>37</td>
<td>77</td>
</tr>
<tr>
<td>surgical failure</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

* POD0 = day of surgery; POD1 = postoperative Day 1.

increased above the preoperative midnight level in 14 of 22 patients in whom surgically induced remission was achieved and in four of five patients who experienced surgical failures (Fig. 1), presumably reflecting the stress of surgery and anesthesia. During the 1st postoperative day, patients in the surgical failure group maintained elevated cortisol levels, presumably due to the continued pattern of cortisol release, surgical manipulation of the tumor, or a combination of both. In every instance, this elevation eliminated the need for exogenous supplementation. The initial surgically induced remission group displayed a notable decline in serum cortisol levels (in 20 of 21 cases there was a decrease from values measured immediately postoperatively to those levels measured at midnight on postoperative Day 1); however, in contrast to earlier reports, this group maintained measurable levels. Significantly, clinical sequelae of steroid insufficiency were not witnessed in either set of patients, though patients in whom disease was in remission were often mildly symptomatic (headache, malaise, or fatigue). All patients were able to tolerate the postoperative period without receiving exogenous steroid medications until the 1st postoperative day. Four of the 22 patients in whom remission was achieved received exogenous steroids following the 6:00 a.m. cortisol measurement, and six patients received exogenous steroids after the noon measurement. The remaining 12 patients tolerated delay past the 6:00 p.m. sample without suffering significant side effects. Withholding cortisol replacement therapy beyond the 1st postoperative day in patients exhibiting mild symptoms of steroid insufficiency was considered to be inappropriate because of the risk of complications from adrenal insufficiency in light of these patients’ suppressed hormonal axes. The data suggest, however, that patients may be safely observed clinically into postoperative Day 1 without corticosteroid supplementation. This practice assumes monitoring in a medical setting by staff members who are well trained in the recognition of and response to endocrinological sequelae of transsphenoidal surgery. Additionally, a clinical laboratory equipped to return accurate and reliable results of serum cortisol samples within less than 24 hours is likewise mandated. Assuming these requirements are met, the data indicate that perioperative corticosteroid therapy is not necessary and testing for surgically induced remission may begin almost immediately following surgery. Advances in determining reliable salivary cortisol levels hold promise for making these measurements more readily available and reliable in the future.

An adequate definition of remission is still under debate. Previous reviewers have consistently acknowledged the significant variety of definitions and their associated pitfalls. Preoperative laboratory and radiological evaluations have been of little predictive value, excluding the decreased likelihood of remission suggested by paradoxical increases of cortisol in response to thyrotropin-releasing hormone and luteinizing hormone–releasing hormone stimulation. Intraoperative evaluation by the surgeon and pathological confirmation of tumor correlate imperfectly with ultimate cure rates. Currently, the most accurate predictors of remission involve quantifiable assays of either postoperative serum cortisol and ACTH levels or postoperative urinary free cortisol excretion. The frequency and timing of collection of such samples varies considerably, and definitions of success found in the literature are diverse, including undetectable postoperative cortisol levels, predefined levels of cortisol, responses to dexamethasone suppression, and combinations of such tests. The data supplied by this study indicate that most patients can be initially stratified into one of two recognizable categories: surgically induced remission or surgical failure. Individuals in whom surgical therapy fails are understandably identified by the fact that they retain both absolutely elevated serum cortisol levels and levels at or above their preoperative nadir value (Fig. 2 and Table 1). Although it is recognized that, in the diseased state, the midnight cortisol level may not represent a true nadir compared with a normal diurnal pattern of cortisol release, these preoperative samples were, in fact, lower than later postoperative values in patients in whom a diseased state was maintained. In contrast, some patients in early remission (14 of 21 cases) exhibited transient elevations in serum cortisol levels soon after surgery (Fig. 2). Serum levels precipitously declined during the 1st postoperative day in 20 of 21 cases, a finding also noted by Arafah, et al. Their analysis, however, was based on macroadenomas and measurements of cortisol levels obtained only once each postoperative morning. Our study differed from that of Arafah, et al., because the concern for steroid insuffi-

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ciency was due not to mass effect from a macroadenoma, but from inhibitory hormonal feedback. Furthermore, as these results indicate, cortisol levels are very dynamic, within even a single 24-hour period.

In our study during the early stage of this postoperative decline (at 6:00 a.m. on postoperative Day 1), only one patient in the initial surgically induced remission group was found to have a serum cortisol level in excess of the preoperative value. At noon none of the patients in the early remission group was found to have a cortisol value in excess of the preoperative midnight cortisol level. In contrast, in four of five patients assigned to the failure group, serum cortisol values at 6:00 a.m. and at noon on postoperative Day 1 were greater than those measured preoperatively. In the only case in which remission was demonstrated at follow-up, the patient, in whom multiple cortisol levels were exhibited in excess of the preoperative level during this window of sampling, was found to experience remission of disease in a delayed fashion (late surgically induced remission). Cortisol levels that are measured below the preoperative midnight value during this period can, therefore, be used to predict surgically induced remission, although they may occasionally appear higher than standard definitions of a cure. Of the 21 patients assigned to the initial remission group, five were found to have one or more serum cortisol measurements greater than or equal to 10 \( \mu g/dl \)—a level that would raise concern for the possibility of incompletely resected tumor. By comparing these levels with the preoperative value and by noting additional cortisol samples lower than 10 \( \mu g/dl \), however, the patients were correctly stratified into the remission group. Although the cortisol levels measured at the 6:00 a.m., noon, and 6:00 p.m. sample points during postoperative Day 1 showed relatively high sensitivities and positive predictive values, the third cortisol level obtained at noon on postoperative Day 1 has the best balance of sensitivity, specificity, positive predictive value, and negative predictive value in estimating surgically induced remission or surgical failure.

The comparison of individual postoperative and preoperative values has the theoretical advantage of monitoring an individual response to surgery, rather than an evaluation based on a comparison to a generalized standard. A situation in which this system might fail, however, would be the severely hypercortisolemic patient who exhibits a drop in postoperative cortisol below the preoperative value but remains absolutely hypercortisolemic. We believe that postoperative cortisol levels do need to fall below 10 \( \mu g/dl \) to satisfy the determination of an initial remission, but data indicate that, under these conditions, such a decrease in cortisol levels is not an absolute requirement.

It was interesting to note the rather narrow range of preoperative midnight cortisol levels in all 27 patients (11–29 \( \mu g/dl \)). Pronounceley elevated cortisol levels may not be as common in Cushing disease as those found in other hormone-secreting adenomas such as prolactinomas. It would appear that, in most cases, this strategy remains valid in evaluating patients for initial surgically induced remissions.

A standard serum cortisol value above and below which all surgical failures and remissions reside, respectively, was not definitely established. As would be expected, however, maintenance of higher serum cortisol values (> 20 \( \mu g/dl \)) during the 1st postoperative day was generally associated with failure, whereas lower levels (< 10 \( \mu g/dl \)) during the same period were associated with remission, although such guidelines were not absolute. Again, all patients, regardless of remission or failure, maintained measurable serum cortisol levels throughout the postoperative testing. Measurable cortisol levels following successful surgery have been reported previously.1-3 Chandler, et al.,4 found that patients with surgically induced remission (tested within 1 week of surgery) had measurable cortisol values in the range of 4.2 ± 3.9 \( \mu g/dl \). Their surgical failure group maintained elevated levels (16 ± 4.7 \( \mu g/dl \)), although these were somewhat lower than the values encountered in the present study.

Although the majority of patients could be classified into the aforementioned groups, this study calls attention to a third pattern of cortisol dynamics. McDonald and associates21 noted two patients in whom cortisol levels failed to be suppressed in response to low-dose dexamethasone following transsphenoidal surgery, signifying continued disease. Ultimately, however, in both cases remission of their disease was achieved without further intervention. A similar response was exhibited by one patient in our study (Fig. 1). We have assigned this pattern the term of “late surgically induced remission.” Using the criteria previously mentioned (elevation of serum cortisol above the preoperative value and > 10 \( \mu g/dl \) on the 1st postoperative day between 6:00 a.m. and noon), we assigned this patient to the initial surgical failure group. During later evaluation, however, the patient’s disease was found to be in remission despite the lack of additional therapy. Although this patient was not challenged with dexamethasone, as were those patients in McDonald and colleagues’ study, the persistence of elevated postoperative cortisol levels above 10 \( \mu g/dl \) and the fact that two of three samples had cortisol values greater than the preoperative value certainly were indicative of the continued presence of adenoma. Considering these three cases, it appears that a small portion of successfully treated patients continues to secrete ACTH and cortisol in a pattern similar to that of the diseased state. Gradually, this overproduction appears to diminish and cortisol responses normalize. No clear explanation for such a phenomenon is available, although a plausible theory may involve the partial resection of an adenoma, thereby initially allowing for continued hypersecretion. Over time, the tumor may eventually undergo necrosis (theoretically due to mechanical injury and/or vascular interruption) and the patient thereby experiences disease remission in a delayed fashion.19,20 In this study we can only hypothesize about the mechanism in these patients, but the fact remains that such a pattern exists. The vital importance of closely following these patients is emphasized to lessen the chance of administering unnecessary therapy. This phenomenon has been identified rarely and, therefore, cannot be accurately predicted. Patients in whom moderately elevated cortisol levels (> 10 \( \mu g/dl \)) and < 20 \( \mu g/dl \) are demonstrated, however, may benefit from follow-up endocrinological testing, rather than immediate reoperation. Additional criteria (surgeon’s estimation of tumor resection and pathological confirmation of resection) might also prove helpful in separating cases of surgical failures, which require further therapy, from those exhibiting the late remission pattern.
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Last, it must be acknowledged that our study offers a novel insight into early postoperative cortisol dynamics but cannot definitively be used to comment on absolute recurrence rates. The follow-up period is admittedly limited and, although initial classifications do appear to hold true for the studied time periods in the majority of patients, a longer postoperative period is required before a truly accurate assessment of long-term surgical cure rates can be made. The study size of the surgical failures was also notably limited and restricts the analysis of such data.

Conclusions

By examining the preoperative state and postoperative response of serum cortisol in patients undergoing surgical resection of ACTH-producing pituitary adenomas, several conclusions may be made. Perioperative steroid medications, at least those continued into the 1st postoperative day, are not routinely required and merely serve to extend the interval between surgery and accurate testing for disease remission. Furthermore, the classification of patients into remission or no remission groups perhaps oversimplifies the possible outcomes from surgery. Indeed, in the majority of patients evidence of immediate disease remission is shown following surgery, whereas in others therapy has obviously failed. A third group of patients, albeit a minority, may initially appear to have been unsuccessfully treated, only to have serum cortisol levels normalize in a delayed fashion. When deciding on immediate reoperation or adjunctive therapy for surgical failures we must therefore be mindful of such a group, to avoid unnecessary treatment for these patients.

We also suggest that initial remission be defined on the basis of two criteria: 1) a comparison between serum cortisol levels measured from 6:00 a.m. to 6:00 p.m. on postoperative Day 1 and serum cortisol levels measured at midnight preoperatively, given that perioperative exogenous steroid administration is withheld; and 2) maintenance of cortisol levels at or below 10 μg/dl throughout two or more of these specific samples. In cases of surgical failures serum cortisol levels are often found above preoperative values and in excess of 20 μg/dl. The advantages of using such a system are multiple. The minimal time from operation to testing allows for a more expedient postoperative case management. Additionally, these criteria take into account studies demonstrating measurable cortisol levels following surgery in patients in whom remission of disease was achieved. No provocative testing is required using these methods, thereby minimizing the manpower and expense required to evaluate the patients. By obtaining the midnight preoperative value for a comparison with postsurgical cortisol levels, the surgeon is able to assess the cortisol dynamics of each patient independently. Before instituting further therapy in patients whose surgery has presumably failed, the physician must consider the possibility that the patient may experience disease remission in a delayed fashion. This may be suggested by moderately elevated postoperative cortisol levels (> 10 μg/dl and < 20 μg/dl), although such proof is unavailable. Unless the postoperative hypercortisolism is similar to that seen preoperatively, monitoring for several weeks before further intervention is implemented might be advisable.

At present, a definitive postoperative test conveying absolute sensitivity and specificity for the outcome of surgically treated Cushing disease is not available. Obviously, serial testing of patients will heighten the sensitivity and specificity of the separation of surgically induced remissions from surgical failures. The concern of mistaking cyclic cortisol secretion or a late remission for a surgical failure virtually mandates such a practice. With inpatient stays being continually shortened, however, a faster, more efficient testing method is desirable, assuming that appropriate facilities are available. Although all these patients need to be monitored for long-term remissions, the methods outlined earlier appear to take into account each individual’s cortisol burden and allow for a rapid evaluation in the immediate and early postoperative period.

References


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