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The impact of peri-operative dexamethasone administration on the normal hypothalamic pituitary adrenal response to major surgical procedures.
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BACKGROUND: Surgical procedures are associated with activation of the hypothalamic-pituitary-adrenal axis (HPA). Studies examining HPA dynamics peri-operatively are limited and the modulating influence of peri-operatively administered glucocorticoids on that is not well established. This investigation examined alterations in HPA function and the impact of dexamethasone (DEX) administration during the peri-operative period.

METHODS: We examined HPA function in 297 patients with normal function who had surgical procedures including pituitary mass resection (n = 191), craniotomy (n = 17) and other thoracic/abdominal/pelvic surgeries (n = 89). HPA function was assessed by frequent measurements of parameters defining adrenal function: ACTH, cortisol, DHEA and DHEA-S levels for 48 h. DEX was administered as a single dose (2-10 mg) to 30 and as multiple doses (12-36 mg) to 21 patients. The data of DEX-treated subjects within each group were similar and were combined together.

RESULTS: Pre-operative data were similar for patients having different surgical procedures. Without DEX exposure, ACTH increased to 225 ± 100 ng/L at 2-4 h and gradually declined to baseline values by 36 h while cortisol levels peaked (39.2 ± 13.2 ug/dL) at 6-8 h declining gradually thereafter. Cortisol rise was paralleled by an equimolar increase in DHEA and a subsequent increase in DHEA-S levels. Single doses of DEX did not influence ACTH or cortisol secretion but suppressed the expected rise in DHEA and DHEA-S levels. Multiple doses of DEX suppressed ACTH and cortisol after the 15th postoperative hour and completely blocked the expected rise in DHEA and DHEA-S levels.

CONCLUSIONS: The data provide a detailed overview of HPA function in a large number of subjects who had major surgical procedures. Single and large doses of DEX did not suppress ACTH or cortisol secretion but suppressed adrenal androgen secretion. It took multiple doses of DEX to partially suppress ACTH and cortisol secretion in the peri-operative period.
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Prospective evaluation of a week one overnight metyrapone test with subsequent dynamic assessments of hypothalamic-pituitary-adrenal axis function after pituitary surgery.
Erratum for
Considerations in minimally invasive adrenal surgery; the front- or the backdoor?
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In the last decades, in minimally invasive adrenal surgery, the retroperitoneoscopic adrenalectomy (PRA) has shown favorable results when compared to the laparoscopic transperitoneal adrenalectomy (LTA). However, for many endocrine surgeons it is unclear if, when, and how to transition from LTA to PRA. Although the length of the learning curve for both approaches is comparable, the LTA is a technically more challenging procedure whilst PRA demands an orientation in a new environment in a patient that is positioned upside down. Visiting a proctor is crucial for successfully adopting the PRA procedure, and continued mentorship in a surgeon’s own hospital during the first procedures is preferable. There are several other aspects related to the decision to transition to PRA; the caseload of adrenal patients, learning aspects of other members of the team, technical considerations, case selection, and a well-developed emergency plan in case of complications during surgery. In a dedicated endocrine center with a considerable annual case load of approximately 30 procedures, we recommend to transition to PRA in order to provide the highest quality of care to adrenal patients.
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Ozone-induced systemic effects are modulated through activation of the 
neuro-hormonal stress response pathway. Adrenal demedullation (DEMED) or 
bilateral total adrenalectomy (ADREX) inhibits systemic and pulmonary effects of 
acute ozone exposure. To understand the influence of adrenal-derived stress 
hormones in mediating ozone-induced lung injury/inflammation, we assessed global 
gene expression (mRNA sequencing) and selected proteins in lung tissues from male 
Wistar-Kyoto rats that underwent DEMED, ADREX, or sham surgery (SHAM) prior to 
their exposure to air or ozone (1ppm), 4h/day for 1 or 2 days. Ozone exposure 
significantly changed the expression of over 2300 genes in lungs of SHAM rats, 
and these changes were markedly reduced in DEMED and ADREX rats. SHAM surgery but 
not DEMED or ADREX resulted in activation of multiple ozone-responsive pathways, 
including glucocorticoid, acute phase response, NRF2, and PI3K-AKT. Predicted 
targets from sequencing data showed a similarity between transcriptional changes 
induced by ozone and adrenergic and steroidal modulation of effects in SHAM but 
not ADREX rats. Ozone-induced increases in lung Il6 in SHAM rats coincided with 
neutrophilic inflammation, but were diminished in DEMED and ADREX rats. Although 
ozone exposure in SHAM rats did not significantly alter mRNA expression of Ifnγ 
and Il-4, the IL-4 protein and ratio of IL-4 to IFNγ (IL-4/IFNγ) proteins 
increased suggesting a tendency for a Th2 response. This did not occur in ADREX 
and DEMED rats. We demonstrate that ozone-induced lung injury and neutrophilic 
inflammation require the presence of circulating epinephrine and corticosterone, 
which transcriptionally regulates signaling mechanisms involved in this response. 

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Androstenedione and 17-α-Hydroxyprogesterone Are Better Indicators of Adrenal 
Vein Sampling Selectivity Than Cortisol. 
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For identification of potentially surgically curable primary aldosteronism, 
guidelines recommend use of adrenal vein sampling (AVS) that requires selective 
catheterization of both adrenal veins as verified by using the cortisol-derived 
selectivity index. Unfortunately, bilaterally selective studies are not obtained 
under unstimulated conditions in a proportion of the cases ranging between 15%
and 50% depending on the cutoff used. We therefore investigated whether 17-α-hydroxyprogesterone and androstenedione, which showed a higher step-up between adrenal vein and inferior vena cava blood than cortisol, can ascertain selectivity when cortisol failed to do so. We prospectively recruited 32 hypertensive patients with confirmed primary aldosteronism, who underwent bilaterally simultaneous sampling without cosyntropin stimulation and with the same predefined AVS protocol. All were consecutively selected because of a cortisol-based selectivity index <2.00 in at least one of the paired adrenal vein blood samples collected as per protocol. Results showed that the values of the selectivity index based on 17-α-hydroxyprogesterone and androstenedione were higher (P<0.01) on average by 1.6- and 12-fold, respectively, than those based on cortisol. With use of these steroids, we rescued 43% and 73% of the AVS, respectively, from being judged nonselective. Thus, in challenging patients with primary aldosteronism submitted to AVS use of 17-α-hydroxyprogesterone, and even more so of androstenedione, for ascertaining selectivity allows demonstration of correct catheter placement in a proportion of AVS studies better than cortisol. Thus, replacing cortisol measurement with these steroids, and particularly androstenedione, can improve the diagnostic yield of AVS.

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A case of long-term survival after surgical resection for solitary adrenal recurrence of esophageal squamous carcinoma.
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BACKGROUND: Esophageal carcinomas are highly malignant tumors with a high frequency of lymph node and distant organ metastasis. Treatment for recurrent tumors is generally decided on an individual basis. Although multidisciplinary treatments involving chemotherapy, surgical resection, and radiation are performed, the prognosis remains poor. Here, we report a case of prolonged recurrence-free survival (38 months) after esophageal carcinoma surgery and subsequent laparoscopic adrenalectomy for right adrenal metastasis.

CASE PRESENTATION: An 83-year-old man was diagnosed with type 3 esophageal squamous cell carcinoma (T3N1M0, cStage IIIA, UICC-7), spreading from the lower thoracic esophagus to the abdominal esophagus. He underwent thoracoscopic esophagectomy with a two-field lymph node dissection followed by substernal gastric tube reconstruction. The final diagnosis was moderately differentiated squamous cell carcinoma (T3N2M0, fStage IIIB). Adjuvant chemotherapy was not administered because of the advanced age and postoperative condition of the
Patient. Computed tomography (CT) at 14 months postoperatively showed a mass with a 2-cm diameter at the right adrenal gland. Positron emission tomography (PET)/CT revealed a high fluorodeoxyglucose (FDG) uptake in the mass. It was suspected that the mass was a metastatic lesion secondary to the primary esophageal carcinoma. No metastases to lymph nodes or other distant organs were identified. The patient underwent laparoscopic right adrenalectomy. The histopathological examination revealed moderately differentiated squamous cell carcinoma, suggesting metastasis from the primary esophageal carcinoma. He has survived without recurrence for 38 months since laparoscopic adrenalectomy to remove the right adrenal metastatic mass after the esophageal carcinoma surgery.

CONCLUSIONS: We describe a very elderly male who survived laparoadrenalectomy for right adrenal metastasis following esophageal cancer surgery without recurrence for 38 months postoperatively. Therefore, surgical resection might be an option for solitary adrenal recurrence.

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Letter to the Editor Regarding Article, "Assembling a Functional Clitoris and Vulva from a Pseudo-Penis: A Surgical Technique for an Adult Woman with Congenital Adrenal Hyperplasia".
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Posterior retroperitoneoscopic adrenal surgery for clinical and subclinical Cushing’s syndrome in patients with bilateral adrenal disease.
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BACKGROUND: The treatment of hypercortisolism for patients with bilateral adrenal disease (BAD) is controversial. Bilateral total adrenalectomy results in permanent hypocortisolism requiring lifelong steroid replacement. A more
conservative surgical approach, with less than bilateral total adrenalectomy (leaving functional adrenal tissue either unilaterally or bilaterally), represents an alternative option; however, long-term outcome or recurrence data are limited. We report our experience with the surgical management of hypercortisolism caused by BAD.

METHODS: Between 2004 and 2016, 42 patients (12 male, 30 female; mean age 58 ± 10 years) with clinical or subclinical Cushing’s syndrome (CS/sCS) caused by BAD underwent adrenal surgery via the posterior retroperitoneoscopic approach. Adrenal surgery was defined as "adrenalectomy" when total gland excision was performed or "resection" when a partial or subtotal adrenal resection was performed. Clinical, radiological and biochemical parameters were evaluated preoperatively and postoperatively.

RESULTS: Seventy adrenal operations performed in total included unilateral resection (n = 3), unilateral adrenalectomy (n = 15), bilateral resection (n = 9), adrenalectomy and contralateral resection (n = 14) and bilateral total adrenalectomy (n = 3). Median operating time was 47.5 min (30-150) with no difference between unilateral and bilateral (synchronous included) procedures (p = 0.15). Mortality was zero. Clavien-Dindo grade of postoperative complications was I (n = 5) and IV (n = 3). All but one patient with CS and 17/31 patients with sCS received postoperative steroid supplementation for a median duration of 20 (1.5-129) months. After median follow-up of 40 months (3-129), the remission rate was 92%; 11 patients required ongoing steroid supplementation. There were three biochemical recurrences (two underwent contralateral resection); two patients with new/progressive radiological nodularity are biochemically eucortisolaemic. A significant reduction in BMI (p = 0.01) and antihypertensive requirements (p = 0.04) was observed postoperatively.

CONCLUSION: A surgical approach which facilitates the conservation of functional adrenal tissue represents a suitable strategy for hypercortisolism caused by BAD. This approach avoids the necessity for lifelong steroid replacement in the majority of cases with low rates of adrenal insufficiency and recurrence.

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