

1. Endocrinol Metab Clin North Am. 2019 Dec;48(4):875-885. doi: 10.1016/j.ecl.2019.08.014. Epub 2019 Sep 25.

Surgical Approach to Endocrine Hypertension in Patients with Adrenal Disorders.

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Increased hormonal secretion of aldosterone, cortisol, or catecholamines from an adrenal gland can produce a variety of undesirable symptoms, including hypertension, which may be the initial presenting symptom. Consequences of secondary hypertension can result in potential cardiovascular and cerebrovascular complications at higher rates than in those with essential hypertension. Once a biochemical diagnosis is confirmed, targeted pharmacotherapy can be initiated to improve hypertension and may be corrected with surgical intervention. Adrenalectomy can be curative and can reverse the risk of cardiovascular sequelae once blood pressure control is achieved. This article discusses perioperative and operative considerations of adrenal causes of hypertension.

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2. J Clin Endocrinol Metab. 2019 Nov 18. pii: dgz206. doi: 10.1210/clinem/dgz206. [Epub ahead of print]

Dynamic pituitary-adrenal interactions in the critically ill after cardiac surgery.

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CONTEXT: Patients with critical illness are thought to be at risk of adrenal insufficiency. There are no models of dynamic hypothalamic-pituitary-adrenal (HPA) axis function in this group of patients and thus current methods of diagnosis are based on aggregated, static models.

OBJECTIVE: To characterise the secretory dynamics of the HPA axis in the critically ill after cardiac surgery.

DESIGN: Mathematical modelling of cohorts.

SETTING: Cardiac critical care unit.

PATIENTS/SUBJECTS: 20 male patients critically ill (CI) at least 48 hours after cardiac surgery and 19 healthy (H) male volunteers.

INTERVENTIONS: None.

MAIN OUTCOME MEASURES: Measures of hormone secretory dynamics were generated from serum adrenocorticotrophic hormone (ACTH) sampled every hour and total cortisol every 10-minutes for 24-hours.

RESULTS: All critically ill patients had pulsatile ACTH and cortisol profiles.

Critically ill patients had similar ACTH secretion (1036.4(737.6)pg/ml/24hrs) compared to the healthy volunteers (1502.3(1152.2)pg/ml/24hrs, $p=0.2$), but increased cortisol secretion (CI:14447.0(5709.3) v H:5915.5(1686.7)nmol/L/24hrs, $p<0.0001$). This increase in cortisol was due to non-pulsatile (CI:9253.4(3348.8) v H:960(589.0)nmol/L/24hrs, $p<0.0001$), rather than pulsatile cortisol secretion (CI:5193.1(3018.5) v H:4955.1(1753.6)nmol/L/24hrs, $p=0.43$). Seven (35%) of the 20 CI patients had cortisol pulse nadirs below the current international guideline threshold for Critical Illness Related Corticosteroid Insufficiency, but an overall secretion that would not be considered deficient.

CONCLUSIONS: This study supports the premise that current tests of HPA axis function are unhelpful in the diagnosis of adrenal insufficiency in the critically ill. The reduced ACTH and increase in non-pulsatile cortisol secretion imply that the secretion of cortisol is driven by factors outside the HPA-axis in critical illness.

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The Influence of Persistent Organic Pollutants on Thyroidal, Reproductive and Adrenal Hormones After Bariatric Surgery.

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INTRODUCTION: Persistent organic pollutants (POPs) including organochlorine pesticides, polychlorinated biphenyls (PCBs), and per- and polyfluoroalkylated substances (PFASs) are suspected endocrine disruptors.

AIM: To evaluate the associations between POPs and thyroidal, reproductive, and adrenal hormones in a study population treated with bariatric surgery.

METHODS: Blood samples from a cohort of 63 participants before and 1 year after bariatric surgery were analyzed for 16 lipophilic POPs, 17 PFASs, and thyroidal, reproductive, and adrenal hormones. Participants reporting relevant medical conditions or interfering medication were excluded, and plausible confounders were corrected for in multiple regression analyses.

RESULTS: Free thyroxine (fT4) showed a significant decrease from preoperative to postoperative follow-up, and regression analyses demonstrated that p,p'-dichlorodiphenyldichloroethylene (p,p'-DDE) was inversely associated with the ratio free triiodothyronine/free thyroxine (fT3/fT4). Testosterone concentrations in male participants increased significantly in the study period, and sex hormone-binding globulin (SHBG) increased in both gender. Regression analyses showed positive associations between increased levels of lipophilic POPs and the raised postoperative testosterone and SHBG concentrations in males. For females, an inverse association between the sum perfluoroalkyl carboxylic acids (Σ PFCA) and SHBG was seen. Regression analyses of postoperative serum cortisol concentrations on changes in hexachlorobenzene (HCB) showed a non-significant inverse association.

CONCLUSION: The results suggest that POPs may have an influence on the hypothalamic-pituitary-thyroid (HPT) and the hypothalamic-pituitary-gonadal (HPG) axes after bariatric surgery. Because of small sample sizes and discrepancy in the sampling time points pre- and postoperatively, the observed hormonal impacts of POPs must be interpreted as associative and not causative. Further studies are needed to confirm the findings.

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4. Langenbecks Arch Surg. 2019 Nov 7. doi: 10.1007/s00423-019-01827-5. [Epub ahead of print]

Volume-outcome correlation in adrenal surgery-an ESES consensus statement.

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BACKGROUND: Published data in the last decade showed that a majority of adrenal operations are done by surgeons performing only one such case per year and based on the distribution of personal workloads 'high-volume' surgeons are defined as those doing 4 or more cases/year.

PURPOSE: This paper summarises literature data identified by a working group

established by the European Society of Endocrine Surgeons (ESES). The findings were discussed during ESES-2019 conference and members agreed on a consensus statement.

RESULTS: The annual of adrenal operations performed yearly in individual countries was reported to be 800/year in UK and over 1600/year in France. The learning curve of an individual surgeon undertaking laparoscopic, retroperitoneoscopic or robotic adrenalectomy is estimated to be 20-40 cases. Preoperative morbidity and length of stay are more favourable in high-volume centres.

CONCLUSION: The main recommendations are that adrenal surgery should continue only in centres performing at least 6 cases per year, surgery for adrenocortical cancer should be restricted to centres performing at least 12 adrenal operations per year, and an integrated multidisciplinary team should be established in all such centres. Clinical information regarding adrenalectomies should be recorded prospectively and contribution to the established EUROCRINE and ENSAT databases is strongly encouraged. Surgeons wishing to develop expertise in this field should seek mentorship and further training from established adrenal surgeons.

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5. Ann Surg. 2019 Nov;270(5):813-819. doi: 10.1097/SLA.0000000000003526.

Adrenalectomy Risk Score: An Original Preoperative Surgical Scoring System to Reduce Mortality and Morbidity After Adrenalectomy.

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OBJECTIVE: To explore the determinants of postoperative outcomes of adrenal surgery in order to build a proposition for healthcare improvement.

SUMMARY OF BACKGROUND DATA: Adrenalectomy is the recommended treatment for many benign and malignant adrenal diseases. Postoperative outcomes vary widely in the literature and their determinants remain ill-defined.

METHODS: We based this retrospective cohort study on the "Programme de

médicalisation des systèmes d'information" (PMSI), a national database that compiles discharge abstracts for every admission to French acute health care facilities. Diagnoses identified during the admission were coded according to the French adaptation of the 10th edition of the International Classification of Diseases (ICD-10). PMSI abstracts for all patients discharged between January 2012 and December 2017 were extracted. We built an Adrenalectomy-risk score (ARS) from logistic regression and calculated operative volume and ARS thresholds defining high-volume centers and high-risk patients with the CHAID method. RESULTS: During the 6-year period of the study, 9820 patients (age: 55 ± 14; F/M = 1.1) were operated upon for adrenal disease. The global 90-day mortality rate was 1.5% (n = 147). In multivariate analysis, postoperative mortality was independently associated with age ≥75 years [odds ratio (OR): 5.3; P < 0.001], malignancy (OR: 2.5; P < 0.001), Charlson score ≥2 (OR: 3.6; P < 0.001), open procedure (OR: 3.2; P < 0.001), reoperation (OR: 4.5; P < 0.001), and low hospital caseload (OR: 1.8; P = 0.010). We determined that a caseload of 32 patients/year was the best threshold to define high-volume centers and 20 ARS points the best threshold to define high-risk patients. CONCLUSION: High-risk patients should be referred to high-volume centers for adrenal surgery. DOI: 10.1097/SLA.00000000000003526 PMID: 31592809

6. Eur Urol. 2019 Nov;76(5):e144-e145. doi: 10.1016/j.eururo.2019.08.002. Epub 2019 Sep 13.

Reply to Franco Gaboardi, Guglielmo Mantica, and Nazareno Suardi's Letter to the Editor re: Giuseppe Simone, Umberto Anceschi, Gabriele Tuderti, et al.

Robot-assisted Partial Adrenalectomy for the Treatment of Conn's Syndrome: Surgical Technique, and Perioperative and Functional Outcomes. Eur Urol 2019;75:811-6.

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7. Eur Urol. 2019 Nov;76(5):e142-e143. doi: 10.1016/j.eururo.2019.08.003. Epub 2019 Aug 16.

Re: Giuseppe Simone, Umberto Anceschi, Gabriele Tuderti, et al. Robot-assisted Partial Adrenalectomy for the Treatment of Conn's Syndrome: Surgical Technique, and Perioperative and Functional Outcomes. Eur Urol 2019;75:811-6.

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PMID: 31427123

8. Curr Opin Oncol. 2019 Oct 18. doi: 10.1097/CCO.0000000000000594. [Epub ahead of print]

Adrenal tumours: open surgery versus minimally invasive surgery.

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PURPOSE OF REVIEW: The aim of this article is to focus on state-of-the-art minimally invasive adrenalectomy (MIA) and the most recent role of open adrenalectomy for adrenal tumours, respect to MIA and open adrenalectomy for adrenocortical cancer (ACC).

RECENT FINDINGS: The laparoscopic (both transperitoneal and retroperitoneal) approach is the first-choice treatment in cases of small-to-medium benign adrenal tumours. This approach is feasible and well tolerated even for larger lesions without radiological signs of malignancy. Robotic adrenalectomy has recently increased in popularity, although the results appear to be fully comparable with those of laparoscopy. Open approach is the keystone of ACC surgery, especially when neighbour tissues, organs, or vessels are involved. Recent evidence suggests caution in treating localized ACC with laparoscopy, because of the higher rate of local or peritoneal recurrence, and shorter recurrence-free survival rates with respect to open adrenalectomy.

SUMMARY: MIA has progressively replaced the traditional open approach and plays a complementary role in the treatment of adrenal tumour. It is the first option for benign lesions, whereas open adrenalectomy is a cornerstone treatment for ACC. The overlap of indications for laparoscopic adrenalectomy and open adrenalectomy is today confined to the treatment of organ-confined adrenal cancer, in which the role of laparoscopic surgery is far from being clearly defined.

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9. J Laparoendosc Adv Surg Tech A. 2019 Oct 15. doi: 10.1089/lap.2019.0554. [Epub ahead of print]

Comparison of Cosmetic Effect and Pain Reduction Outcomes of Modified Mini-Laparoscopy Versus Laparoendoscopic Single-Site Surgery for Adrenalectomy.

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Objective: This study was to introduce the modified mini-laparoscopic adrenalectomy and investigate the advantage of operative time, cosmetic effect, and pain reduction by comparing the modified mini-laparoscopic adrenalectomy and laparoendoscopic single-site surgery (LESS). **Methods and Patients:** Between May 2015 and Jun 2018, 76 consecutive patients with adrenal tumor underwent laparoscopic adrenalectomy. Of which, 36 cases were in the mini-laparoscopic surgery group (the M group) and 40 cases in the LESS group. Medical records of the consecutive patients were analyzed. The operative time, blood loss, the Visual Analog Scale (VAS) scores and the Scar Cosmesis Assessment and Rating

(SCAR) Scale scores were recorded. Results: The mean operative time in the M group was significantly less than that of in the LESS group (54.75 ± 9.37 min vs. 106.48 ± 19.71 min, $P < .01$). Mean estimated blood loss did not differ between the 2 groups (12.22 ± 5.29 mL vs. 10.80 ± 6.66 mL, $P > .05$). The mean VAS scores in the M group were significantly lower than those of the LESS group on postoperative days (POD) 1 and 3. The SCAR scale scores at POD 60 were similar in the M group and the LESS group (0.86 ± 0.64 vs. 0.95 ± 0.71 , $P > .05$).

Conclusions: Modified mini-laparoscopic adrenalectomy is safe and convenient. It offered less operative time, significant cosmetic benefit, and reduced incisional pain.

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10. J Pediatr Urol. 2019 Oct 10. pii: S1477-5131(19)30311-0. doi:

10.1016/j.jpuro.2019.09.022. [Epub ahead of print]

Beyond changing diapers: stress and decision-making among parents of girls with congenital adrenal hyperplasia seeking consultation about feminizing genital restoration surgery.

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INTRODUCTION/BACKGROUND: The impact of having a child with atypical genitalia due to a life-threatening chronic medical condition like congenital adrenal hyperplasia (CAH) is poorly understood.

OBJECTIVE: The aim of the study was to determine parental stress and impact of CAH on parental decisions, including decisions regarding female genital restoration surgery (FGRS).

STUDY DESIGN: The authors surveyed consecutive parents of girls with CAH ≤ 3 years presenting at a tertiary referral center for FGRS consultation (2016-2019). The survey was developed by three families of daughters with CAH and six clinicians. Nine potentially stressful past experiences were rated on a 6-point Likert scale ('not at all' to 'extremely' stressful). Overall parental stress and strain (broader negative consequences) were reported using validated instruments (Perceived Stress Scale and Caregiver Strain Questionnaire Short Form, respectively). Impact of CAH on past decisions about childcare, social interactions, and who changes diapers were also assessed. Non-parametric tests were used for analysis.

RESULTS: Twenty-nine parents (median age: 32years) of 22 consecutive children participated (Prader 3/4/5: 59.1%/36.4%/4.5%). After the study, 20 girls (90.9%) underwent FGRS at a median age of 8 months. The most stressful experiences were having an adrenal crisis ('very much' stressful), waiting for the CAH diagnosis, and making sense of the diagnosis (both 'quite a bit') (Figure 1). Remaining issues were 'somewhat' stressful. Deciding whether to proceed with FGRS was ranked as the least stressful issue. Overall parental stress was similar to overall stress previously reported by spousal caregivers of stroke or heart failure survivors ($P \geq 0.15$). Overall parental strain was similar to parents of

adolescents receiving mental health counseling ($P = 0.77$). Congenital adrenal hyperplasia impacted decisions about babysitting, daycare, who changed diapers, and choosing a pediatrician ($P \leq 0.02$), but did not impact parental social interactions ($P \geq 0.11$). Diapers were typically changed by parents (100.0%) and grandmothers (50.0%). Parents anticipated that some individuals currently not allowed to change diapers would be allowed after FGRS: grandfathers (+18.2%), aunts/uncles (+27.3-32.8%), cousins (+18.2%), and family friends (+45.5%).

DISCUSSION: The authors present the first assessment of parental stress with respect to different aspects of care of a daughter with CAH. Larger studies are required to determine if the parental stress associated with these experiences varies over time and how these stressors rank relative to each other through the child's development.

CONCLUSION: Parents experience multiple stressors after having a daughter with CAH. Parental stress surrounding a decision about FGRS appears less severe than events pertaining to the diagnosis and medical management of CAH. Congenital adrenal hyperplasia impacts multiple parental decisions.

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11. Kardiochir Torakochirurgia Pol. 2019 Oct;16(3):118-123. doi: 10.5114/kitp.2019.88600. Epub 2019 Oct 28.

Assessment of adrenal reserve and secretion of cortisol in patients over 60 years of age undergoing cardiac surgery.

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Introduction: Cortisol level affects the prognosis of patients after cardiac surgery. Meanwhile, there are no clear guidelines for steroid supplementation after a cardiac operation. The relationship between age and blood cortisol levels has not been finally clarified.

Aim: Assessment of adrenal reserve and secretion of cortisol in patients over 60 years of age undergoing cardiac surgery.

Material and methods: The study included 20 patients of both sexes referred for cardiac surgery. A short ACTH synthetic stimulation test was carried out.

Assessment of cortisol secretion was carried out in the morning on the day of surgery and the 1st, 2nd and 4th days after surgery in blood samples.

Results: A result within the normal range for the adrenal reserve was found in 19 of the 20 patients enrolled in the study. The short Synacthen test predicted postoperative secretion of cortisol ($p = 0.04$, $r = 0.047$). A relationship between secretion of cortisol and patients' age was observed ($p = 0.03$, $r = 0.48$). The concentration of cortisol on the 1st postoperative day was correlated with the total dose of dopamine ($p = 0.006$, $r = 0.58$) and adrenaline ($p = 0.04$, $r = 0.47$). The concentration of cortisol on the day of the surgery correlated with the lactate concentration on day 2 ($p = 0.04$, $r = 0.45$). The concentration of

lactates on day 1 correlated with total dose of dopamine ($p = 0.01$, $r = 0.54$).
Conclusions: A short Synacthen test allows one to predict secretion of cortisol after cardiac surgery. Greater secretion of cortisol after cardiac surgery may be associated with a more difficult postoperative course. There was no decrease in cortisol secretion with age.

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Conflict of interest statement: The authors report no conflict of interest.

12. European J Pediatr Surg Rep. 2019 Jan;7(1):e75-e78. doi: 10.1055/s-0039-1694058. Epub 2019 Oct 31.

Minimally Invasive Surgery for Pediatric Adrenal Masses-Report on Four Cases.

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The dignity of adrenal masses in children varies from benign lesions like adenoma and ganglioneuroma to malignant tumors like adrenocortical carcinoma and neuroblastoma. Any surgical approach, especially minimally invasive surgery (MIS), requires careful risk stratification based on oncological and technical criteria. Herein, we present four patients who underwent MIS for adrenal masses. Laboratory testing differentiated between simple cysts and adenoma, but could not identify a child with adrenocortical tumor preoperatively. Analysis of image-defined risk factors excluded vascular encasement in all cases. All patients underwent laparoscopic adrenalectomy without complications. Histopathology revealed simple cyst, ganglioneuroblastoma, adenoma, and potentially malignant adrenocortical tumor in one patient/case each. All specimen showed clear margins and no recurrence was noted at a mean follow-up of 18 months.

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