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Adrenal vein sampling with and without cosyntropin stimulation for detection of surgically remediable aldosteronism.

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Context and Objective: Bilateral adrenal vein sampling (AVS), the diagnostic standard for identifying surgically remediable aldosteronism (SRA), is commonly performed after cosyntropin stimulation (post-ACTHstim). The role of AVS without cosyntropin stimulation (pre-ACTHstim) has not been established. The selectivity index (SI), the adrenal vein (av) serum cortisol concentration divided by that in a peripheral vein, confirms av sampling. The minimally acceptable SI is controversial. The objectives of this study were to determine the role of pre-ACTHstim AVS and a predetermined SI.

Design: Using biochemical cure as the endpoint, we performed a retrospective head-to-head comparison of pre-ACTHstim AVS to post-ACTHstim AVS. The specificity of a predetermined minimum SI of 1.5 in pre-ACTHstim AVS was determined.

Patients: At a regional AVS referral centre, we analysed 32 patients who had undergone simultaneous bilateral AVS both pre- and post-ACTHstim and had returned for postadrenalectomy evaluation.

Measurements: Simultaneous bilateral AVS was performed with measurements of venous concentrations of aldosterone and cortisol. End points were postadrenalectomy plasma renin activity, serum aldosterone concentration, and number of antihypertensive medications.

Results: All 32 patients achieved a biochemical cure following adrenalectomy. The two AVS protocols were complementary. Notably, seven patients (22%; CI = 11-38) were found to have SRA by a lateralization index (LI) > 4 on the pre-ACTHstim AVS, but not on the post-ACTHstim AVS. SI pre-ACTHstim was divided into tertiles. Specificity was 100% in all.

Conclusions: Simultaneous bilateral AVS performed both pre-ACTHstim and post-ACTHstim maximizes SRA identification. A SI of 1.5 pre-ACTHstim does not reduce specificity.

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Surgery for adrenal angiomyelolipoma: an individualized concept.

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BACKGROUND: Because adrenal angiomyelolipoma (AAML) is rare and uniformly benign, the indications for surgery are ill defined.

METHODS: Among a series of 156 patients with adrenal pathologies surgically treated between 2013 and 2018, 12 patients were operated with the diagnosis of an AAML. The clinical as well as imaging parameters forming the individual indications for surgery were analyzed.

RESULTS: Preoperative diagnosis consistent with AAML was made in all 12 patients. The mean size of surgically removed AAML was 82.3 mm (45-150 mm). Gender and affected side were evenly distributed. Local symptoms but lack of radiological signs suspicious for malignancy or size increase were observed in 4 of 12 patients (group 1, 33%). In contrast, 4 of 12 patients (group 2, 33%) showed radiological signs suspicious for malignancy but lacked local symptoms. Additional 4 of 12 patients (group 3, 33%) showed both local symptoms and radiological signs suspicious for malignancy. Patients with local symptoms harbored significantly larger tumors compared to those patients that lacked local symptoms (93.9 mm \pm 32.8 vs. 59.3 mm \pm 2.7, $p = 0.021$). Patients with radiologically suspicious signs were older (60 years \pm 9.9 vs. 53 years \pm 5.4, $p > 0.05$), and time to surgery was shorter (4.4 months \pm 3 vs. 6.0 months \pm 3.0, $p > 0.05$). Importantly, surgical approach was not influenced by tumor size ($p = 0.65$). However, patients with suspicious imaging were more likely to be operated by conventional open approach (4 of 8 vs. 0 of 4, $p = 0.08$). The minimal invasive approach was associated with shorter hospital stay (7 days, \pm 1.3 vs. 14.2 days, \pm 8.8, $p = 0.038$). All lesions that showed radiological signs suspicious for malignancy proved benign in final histology.

CONCLUSION: Large AAML present a clinical challenge. The presence of local symptoms and/or radiological signs suspicious for malignancy identifies three groups of patients that define the concept of an individualized indication for surgery in AAML. A minimal invasive approach can be advocated even for large AAML with radiological signs suspicious for malignancy.

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Adrenal masses in children: Imaging, surgical treatment and outcome.

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BACKGROUND/OBJECTIVE: This study aims to evaluate the current surgical approach to adrenal masses in the pediatric age group.

METHODS: We retrospectively analyzed cases that underwent surgery for adrenal masses between 2007 and 2017. Patients were assessed regarding age, sex, primary diagnosis, image defined risk factors (IDRF), surgical treatment method, complications, duration of hospital stay, and follow-up.

RESULTS: We examined 50 patients who underwent surgery for adrenal mass (mean age: 4.8 years; range: 5 days-14 years). For IDRF assessment, Ultrasonography was used in 42, Computed Tomography in 36, and Magnetic Resonance Imaging in 36 patients. Lesions were present on the right in 25, left in 21, and bilateral in 4 patients. Histopathological findings were neuroblastoma (n = 29), ganglioneuroma (n = 6), adrenal cortex tumor (n = 5), ganglioneuroblastoma (n = 4), pheochromocytoma (n = 3), cyst (n = 1), and adrenal hematoma (n = 2). Laparotomy was performed on 37 patients, and laparoscopy on 13 patients. None of the cases had any operative complications.

CONCLUSION: The crucial factors determining the surgical approach to adrenal masses in pediatric cases are the histopathology of the mass, volume, and IDRF. Minimally invasive procedures could be reliably performed in appropriate cases.

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Surgical therapy of adrenal tumors: guidelines from the German Association of Endocrine Surgeons (CAEK).

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BACKGROUND AND AIMS: Previous guidelines addressing surgery of adrenal tumors required actualization in adaption of developments in the area. The present guideline aims to provide practical and qualified recommendations on an evidence-based level reviewing the prevalent literature for the surgical therapy of adrenal tumors referring to patients of all age groups in operative medicine who require adrenal surgery. It primarily addresses general and visceral surgeons but offers information for all medical doctors related to conservative, ambulatory or inpatient care, rehabilitation, and general practice as well as pediatrics. It extends to interested patients to improve the knowledge and participation in the decision-making process regarding indications and methods of management of adrenal tumors. Furthermore, it provides effective medical options for the surgical treatment of adrenal lesions and balances positive and negative effects. Specific clinical questions addressed refer to indication, diagnostic procedures, effective therapeutic alternatives to surgery, type and extent of surgery, and postoperative management and follow-up regime.

METHODS: A PubMed research using specific key words identified literature to be considered and was evaluated for evidence previous to a formal Delphi decision process that finalized consented recommendations in a multidisciplinary setting.

RESULTS: Overall, 12 general and 52 specific recommendations regarding surgery for adrenal tumors were generated and complementary comments provided.

CONCLUSION: Effective and balanced medical options for the surgical treatment of adrenal tumors are provided on evidence-base. Specific clinical questions regarding indication, diagnostic procedures, alternatives to and type as well as extent of surgery for adrenal tumors including postoperative management are addressed.

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Minimally Invasive Surgery for Primary and Metastatic Adrenal Malignancy.

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Since the first description of laparoscopic adrenalectomy (LA) for pheochromocytoma and Cushing syndrome in 1992, the utilization of and indications for a minimally invasive approach to the adrenal gland have vastly expanded. Although minimally invasive adrenalectomy has been established as the preferred approach for patients with benign tumors of the adrenal gland, minimally invasive adrenalectomy for cancer remains controversial. In this article, the authors review the indications for minimally invasive adrenalectomy for adrenal nodules suspicious for, or established to represent, a primary malignancy or a site of metastatic cancer.

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Retrospective analysis of variant venous anatomy in 303 laparoscopic adrenalectomies and its clinical implications.

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BACKGROUND AND OBJECTIVES: To clarify the correlation of variant venous anatomy with adrenal tumor phenotype and surgical outcomes.

PATIENTS AND METHODS: This retrospective study included 303 consecutive minimally invasive adrenalectomies from 301 patients. All adrenal veins were identified. We compared the preoperative, intraoperative, and postoperative data between patients with and without variant adrenal venous anatomy. We also explored the factors associated with venous variants.

RESULTS: We found variant venous anatomy in 62 of 303 adrenalectomies (20.5%). Compared with patients with normal anatomy, those with variant anatomy were associated with larger tumor size, larger adrenal veins, more adrenal medullary

tumors, longer operation time, more estimated intraoperative blood loss, longer length of hospitalization, and more transfusion. Computed tomography (CT) images may improve the identification of venous anatomy. Tumor size and diagnosis of pheochromocytoma were independently related to variant venous anatomy, whereas sex, tumor size, and venous variant influenced hemorrhage. For pheochromocytoma with variant venous anatomy operated on by a single surgeon, robot-assisted laparoscopic adrenalectomy was associated with shorter postoperative hospitalization.

CONCLUSIONS: Adrenal vein variants are associated with worse outcomes in adrenal tumors and an optimized surgery strategy should be applied to this group of patients.

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Trends in Adrenal Surgery-The Changing Nature of Tumors and Patients.

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BACKGROUND: The volume of adrenal surgery is increasing. There has been a concern that the widespread use of axial imaging and minimally invasive approaches has led to changing indications for adrenalectomy. We reviewed trends in adrenal surgery at a single academic institution.

MATERIALS AND METHODS: This was a retrospective analysis of all patients who underwent adrenal surgery between 1993 and 2018 by the endocrine surgery service. Patient demographics, diagnosis, operative details, and perioperative complications were evaluated. Trend analysis was performed across ordered year groups (<2000, 2000-2004, 2005-2009, 2010-2014, and 2015-2018).

RESULTS: We identified 732 patients who underwent 751 adrenal operations. Fifty-seven percent of the patients were women, and the median age was 51 y (range: 5-88). There was an increase in the number of procedures performed ($P < 0.01$, trend analysis). Over time, there was a higher proportion of patients with hypertension (54.7% [<2000] versus 73.6% [>2015], $P < 0.01$), diabetes (4.7% versus 22.1%, $P = 0.01$), and classified as American Society of Anesthesiology class 3/4 (15.7% versus 45.7%, $P < 0.01$). More patients had their adrenal lesion found incidentally (19.4% versus 39.3%, $P < 0.01$), and there was a larger proportion of pheochromocytomas (25% versus 36.4%, $P < 0.01$) and fewer nonfunctioning adenomas (7.4% versus 4.3%, $P = 0.03$). Median tumor size decreased from 3.5 cm to 2.9 cm ($P = 0.03$). Complication rates increased over time (8.3% versus 15%, $P < 0.01$), but the overall 30-d mortality remained low (0.3%).

CONCLUSIONS: Adrenal surgery is being performed more commonly with an increasing number of incidentalomas and pheochromocytomas. Our patients have higher comorbidities with increase in complication rates over time, although

perioperative mortality remains low. This highlights the importance of a thorough preoperative evaluation to identify suitable patients who may benefit from adrenalectomy.

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Changes in glucose metabolism based on 75-g oral glucose tolerance tests before and after surgery for adrenal Cushing's syndrome.

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Adrenal Cushing's syndrome (CS) is caused by cortisol-producing adrenal adenoma and is frequently accompanied by glucose metabolism disorders, which are characterized by increased insulin resistance and insufficient β -cell compensation. However, considering the rarity of CS, few studies have assessed whether the glucose metabolism disorders could be ameliorated by surgical treatment. In this case series, we evaluated glucose metabolism before and after surgery in 11 patients (10 women and 1 man) who underwent unilateral adrenalectomy for overt adrenal CS between 2005 and 2016. Patients with pre-diagnosed diabetes mellitus (DM) were excluded. Pre- and post-operative 75-g oral glucose tolerance tests were performed. Cortisol secretion decreased significantly after surgery (median 24-h urinary free cortisol: 582.0 $\mu\text{g/day}$ [interquartile range: 321.0-743.0 $\mu\text{g/day}$] to 31.3 $\mu\text{g/day}$ [23.6-40.6 $\mu\text{g/day}$], $p = 0.001$). The results of the OGTT generally improved after surgery (normal glucose tolerance/impaired glucose tolerance/DM: 2/8/1 to 8/3/0), with significant decreases in the immunoreactive insulin and glucose levels. We also found a decrease in the median homeostatic model assessment of insulin resistance (2.4 [1.4-2.8] to 1.0 [0.6-1.1], $p = 0.002$), and increases in the median Matsuda index (3.0 [2.3-4.5] to 8.2 [6.3-11.4], $p < 0.001$), median insulinogenic index (0.70 [0.22-1.51] to 1.22 [0.78-1.64], $p = 0.08$), and median disposition index (609.1 [237.8-1,095.2] to 1,286.0 [1,034.6-1,857.6], $p = 0.002$). These findings indicate that adrenalectomy for adrenal CS without overt DM may help ameliorate glucose metabolism disorders, and improve both insulin resistance and insulin secretion.

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Robot-assisted Partial Adrenalectomy for the Treatment of Conn's Syndrome: Surgical Technique, and Perioperative and Functional Outcomes.

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BACKGROUND: In the era of minimally invasive surgery, partial adrenalectomy has certainly been underused. We aimed to report surgical technique and perioperative, pathologic, and early functional outcomes of a two-center robot-assisted partial adrenalectomy (RAPA) series.

OBJECTIVE: To detail surgical technique of RAPA for unilateral aldosterone-producing adenoma (UAPA), and to report perioperative and 1-yr functional outcomes.

DESIGN, SETTING, AND PARTICIPANTS: Data of 10 consecutive patients who underwent RAPA for UAPA at two centers from June 2014 to April 2017 were prospectively collected and reported.

SURGICAL PROCEDURE: RAPA was performed using a standardized technique with the da Vinci Si in a three-arm configuration.

MEASUREMENTS: Baseline and perioperative data were reported. One-year functional outcomes were assessed according to primary aldosteronism surgery outcome guidelines. A descriptive statistical analysis was performed.

RESULTS AND LIMITATIONS: All cases were completed robotically. Median nodule size was 18mm (interquartile range [IQR] 16-20). Intraoperative blood loss was negligible. A single (10%) postoperative Clavien grade 2 complication occurred. Median hospital stay was 3 d (IQR 2-3). Patients became normotensive immediately after surgery (median pre- and postoperative blood pressure: 150/90 and 120/70mmHg, respectively). At both 3-mo and 1-yr functional evaluation, all patients achieved biochemical success (aldosterone level, plasmatic renin activity, and aldosterone-renin ratio within normal range). Complete clinical success was achieved in nine patients, but one required low-dose amlodipine at 6-mo evaluation. At a median follow-up of 30.5 mo (IQR 19-42), neither symptoms nor imaging recurrence was observed.

CONCLUSIONS: We demonstrated feasibility and safety of RAPA for UAPA; this technique had very low risk of complications and excellent functional results. Increased availability of robotic platform and increasing robotic skills among urologists make RAPA a treatment option with potential for widespread use in urologic community.

PATIENT SUMMARY: Robot-assisted partial adrenalectomy is a safe, feasible, and minimally invasive surgical approach. Promising perioperative and functional outcomes suggest an increasing adoption of this technique in the near future.

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