Review Articles

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Discrepancies in the Recommended Management of Adrenal Incidentalomas by Various Guidelines

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Abbreviations and Acronyms

AACE/AAES = American Association of Clinical Endocrinologists and American Association of Endocrine Surgeons

ACC = adrenocortical carcinoma

ACR = American College of Radiology

AI = adrenal incidentaloma

AVS = adrenal vein sampling

CT = computerized tomography

CUA = Canadian Urological Association

ESE = European Society of Endocrinology

KES = Korean Endocrine Society

MRI = magnetic resonance imaging

PET = positron emission tomography

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Purpose: Adrenal incidentalomas are being discovered with increasing frequency, and their discovery poses a challenge to clinicians. Despite the 2002 National Institutes of Health consensus statement, there are still discrepancies in the most recent guidelines from organizations representing endocrinology, endocrine surgery, urology and radiology. We review recent guidelines across the specialties involved in diagnosing and treating adrenal incidentalomas, and discuss points of agreement as well as controversy among guidelines.

Materials and Methods: PubMed®, Scopus®, Embase™ and Web of Science™ databases were searched systematically in November 2019 in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement to identify the most recently updated committee produced clinical guidelines in each of the 4 specialties. Five articles met the inclusion criteria.

Results: There is little debate among the reviewed guidelines as to the initial evaluation of an adrenal incidentaloma. All patients with a newly discovered adrenal incidentaloma should receive an unenhanced computerized tomogram and hormone screen. The most significant points of divergence among the guidelines regard reimaging an initially benign appearing mass, repeat hormone testing and management of an adrenal incidentaloma that is not easily characterized as benign or malignant on computerized tomography. The guidelines range from actively recommending against any repeat imaging and hormone screening to recommending a repeat scan as early as in 3 to 6 months and annual hormonal screening for several years.

Conclusions: After reviewing the guidelines and the evidence used to support them we posit that best practices lie at their convergence and have presented our management recommendations on how to navigate the guidelines when they are discrepant.

Key Words: adrenal glands, adrenal gland neoplasms, adrenocortical carcinoma, pheochromocytoma, adrenocortical adenoma

As the quality and resolution of cross-sectional imaging improves, adrenal incidentalomas are detected with increasing frequency. Adrenal incidentalomas, defined as incidentally found adrenal lesions smaller than 1 cm, present diagnostic and management challenges, especially in cases where findings on cross-sectional imaging are nonspecific. Despite the guidelines put forth by the National Institutes of Health and various endocrine, radiological and urological societies, details of the management of adrenal incidentalomas remain controversial. Discrepancies between

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guidelines such as hormonal testing, followup protocols for benign lesions, workup of indeterminate lesions, indications for biopsy and surgical vs nonsurgical management options present nuanced challenges to the provider. Given that interdisciplinary approaches are often necessary in the management of adrenal masses, discordance between guidelines makes coordinated management approaches challenging.

We review the various guidelines for the management of AIs, highlighting their similarities and differences. Guidelines from the following organizations were included: European Society of Endocrinology,[1] Canadian Urological Association,[2] American Association of Clinical Endocrinologists and American Association of Endocrine Surgeons,[3] American College of Radiology[4] and Korean Endocrine Society.[5] Where applicable, we provide an alternative approach to the diagnosis and management of AIs that combines the respective radiological, endocrine and surgical expertise of the societies involved in the care of these patients based on current literature and our multidisciplinary experience at a large academic institution.

METHODS AND MATERIALS

The articles included in this review are the most recently published clinical guidelines from professional organizations representing the specialties that manage AIs, including endocrinology, endocrine surgery, urology and radiology. PubMed, Scopus, Embase and Web of Science databases were searched systematically in November 2019 to identify the most recently updated committee produced clinical guidelines in each of the 4 specialties. Inclusion criteria consisted of clinical guidelines produced from a professional medical association and guidelines from either endocrinology, endocrine surgery, urology or radiology societies. Exclusion criteria consisted of articles published before 2009 and articles that were not the most recent update from an organization. Five articles were identified that met the inclusion and exclusion criteria, and were reviewed. The guidelines set forth in these articles were compared based on their recommendations for radiological and hormonal screening, and followup and management of lesions that appear benign, indeterminate or malignant on CT and are either hormonally functional or nonfunctional.

RESULTS

Initial Evaluation

All 5 guidelines report the necessity of using imaging to describe the adrenal mass as benign or malignant on initial unenhanced CT. The prevailing determinant of benign disease is a mass that has low attenuation, defined as 10 HU or less, which is suggestive of a fat containing adenoma. Additionally a mass greater than 4 cm in diameter is more likely to be malignant. CUA, AACE/AAES, ACR and KES recommend proceeding to enhanced CT with washout if the initial unenhanced CT is equivocal. On enhanced CT with washout an absolute percent washout-to-relative percent washout of 60%:40% or less is suggestive of benign pathology. ESE recommends obtaining second line imaging but could not recommend one specific modality above others, including CT with washout, due to the poor quality of evidence.

After the discovery of an adrenal mass on imaging, all guidelines recommend initial hormonal testing, including a low dose dexamethasone suppression test and plasma-free and/or urinary fractionated metanephrines to rule out a cortisol secreting adenoma and pheochromocytoma, respectively. All reviewed guidelines recommend obtaining an aldosterone-to-renin ratio only if patients have unexplained hypokalemia or hypertension, although none of the guidelines specify which blood pressure parameters or severity of hypertension should be included. Furthermore, if adrenocortical carcinoma is suggested on initial CT, initial testing should include levels of sex hormones and steroid precursors.

Management of a Nonfunctioning, Unilateral Adrenal Mass with Benign Features on Imaging

Although there is consensus among the 5 sets of guidelines that no surgical intervention is indicated for a benign, nonfunctional adrenal mass, followup protocols vary. ESE and ACR guidelines propose that no followup imaging be obtained for a patient with a mass that appears benign on initial CT. AACE/AAES guidelines recommend reimaging the patient in 3 to 6 months and, if there is no radiographic change, reimaging annually for 1 to 2 years. The CUA recommends reimaging the patient 12 months from diagnosis and then following clinically at annual visits for 4 years. KES guidelines suggest repeat CT 12 months after diagnosis and no further followup is necessary if the mass is smaller than 2 cm and there is no change on the followup scan.

ESE does not recommend any additional hormonal testing if the initial hormonal laboratory values were within normal limits. AACE/AAES recommend an annual hormonal panel for 5 years after diagnosis, while CUA recommends annual testing for 4 years and KES recommends annual testing for 4 to 5 years if the tumor is larger than 3 cm.

Management of Nonfunctioning, Unilateral Adrenal Mass with Indeterminate Imaging

Four of the 5 guidelines address indeterminate imaging, and all of these recommend repeat imaging or immediate surgical resection depending on patient preference and overall health. Specifically ESE recommends discussion by a multidisciplinary care

team regarding immediate additional imaging, interval imaging in 6 to 12 months or immediate surgery. The panel did not think there was evidence to justify one of these choices above the others. In the algorithm set forth by the CUA a patient with indeterminate imaging will either receive close followup in 3 to 6 months, a biopsy in rare specific cases or immediate surgical removal. The ACR recommends repeat imaging in 6 to 12 months with unenhanced CT if the patient does not have a cancer history or PET if the patient has active extra-adrenal malignancy. The KES also recommends PET if malignancy is suspected but otherwise recommends repeat CT in 3 to 6 months and annually for 1 to 2 more years. All 4 guidelines recommend surgery if appreciable growth of the mass is seen on repeat imaging.

Management of Unilateral Adrenal Mass with Evidence of Malignancy on Imaging

All 5 guidelines concur that any mass with obvious signs of malignancy on CT where metastasis is considered to be isolated to the adrenal glands should be surgically resected. The reviewed guidelines recommend laparoscopic/robotic adrenalectomy as the modality of choice for smaller and more contained masses, and an open approach for larger and more invasive tumors.

Management of Cortisol Secreting Adenoma

Screening for a cortisol secreting adenoma initially involves measuring the serum cortisol after a 1 mg dexamethasone suppression test. The guidelines use the same scale in which a serum cortisol of 50 nmol/l (1.8 μg/dl) or below excludes autonomous cortisol secretion, 51 to 138 nmol/l (1.9 to 5.0 μg/dl) indicates possible cortisol secretion and above 138 nmol/l (above 5.0 μg/dl) is evidence of autonomous cortisol secretion. All guidelines recommend additional testing for the evaluation of Cushing syndrome when initial screening is abnormal. ESE, AACE/AAES and KES advocate medical screening of comorbid conditions, including hypertension, type 2 diabetes and asymptomatic vertebral fractures in patients newly diagnosed with cortisol secreting adenomas. Adrenalectomy should be considered on an individual patient basis depending on the patient's overall health, symptoms and cortisol induced comorbidities. CUA guidelines claim that adrenal hyperfunctionality is an indication for surgery but there is not enough evidence yet to recommend surgery for every patient.

Management of Pheochromocytoma

Pheochromocytoma must be resected according to the 5 sets of guidelines. Alpha blocker therapy is indicated for 1 to 3 weeks prior to surgery to prevent a catecholamine surge intraoperatively. If necessary, a beta blocker can be added to the regimen to control reflex tachycardia. AACE/AAES guidelines advocate genetic testing for every patient with pheochromocytoma. AACE/AAES guidelines suggest long-term followup for recurrence, and KES guidelines recommend followup for life with biochemical tests.

Management of Aldosterone Secreting Adenomas

AACE/AAES and KES guidelines recommend confirming a diagnosis of primary aldosteronism with a saline challenge, in which intravenous hypertonic saline is administered to a patient and plasma levels of aldosterone, renin and potassium are monitored after several hours. If aldosterone-renin activity fails to decrease after a salt load, the adrenal mass is considered aldosterone producing. AACE/AAES purport that bilateral adrenal vein sampling is an important diagnostic step once hyperaldosteronism has been established. AVS lateralizes the production of aldosterone and can help distinguish between bilateral adrenal hyperplasia and a unilateral adenoma. AACE/AAES recommend utilizing AVS in the majority of patients, even those with masses well visualized on imaging. The KES does not comment on the utility of AVS. AACE/AAES, CUA and KES advocate for laparoscopic adrenalectomy in the case of an aldosterone secreting adenoma. When surgery is not possible or is not indicated by AVS, patients should be treated with a mineralocorticoid receptor antagonist.

Management of Bilateral AIs

ESE and KES address the management of bilateral adrenal incidentalomas. These guidelines recommend working up and treating each mass individually with the protocol described above. As an exception, ESE recommends against bilateral adrenalectomy for asymptomatic cortisol secreting adenomas. In rare cases, notably bilateral pheochromocytomas in a patient with a genetic syndrome, these guidelines allow for partial adrenalectomy to be considered. Both guidelines also advise collecting 17-hydroxyprogesterone levels to rule out congenital adrenal hyperplasia.

Special Populations

ESE and KES recommend urgent assessment for pregnant women, children and all people younger than 40 years old due to the greater risk of adrenal malignancy in this population. MRI is the preferred screening modality for this population and should be used instead of CT when possible. According to ESE and KES, quality of life and medical comorbidities should be considered with regard to management options for elderly patients with newly discovered adrenal masses.

History of Malignancy

ESE and KES guidelines recommend excluding pheochromocytoma even if the mass is likely to be metastasis in a patient with a history of malignancy.

After that they recommend followup PET, except for lesions characterized as benign on CT, which require no further workup. AACE/AAES, CUA and ACR also suggest that PET is a useful next step in a patient with a newly discovered adrenal mass and history of malignancy. ESE, AACE/AAES and KES all recommend assessing adrenal function in patients with bilateral metastasis.

Indications for Biopsy

All 5 guidelines stipulate that biopsy is of limited clinical value and should not be part of an initial workup. ESE and KES recommend biopsy only in the case of a hormonally inactive mass with nonbenign imaging in which pathology results would directly change management. AACE/AAES guidelines suggest that biopsy is useful only in rare instances in which it is necessary for staging and treatment. CUA and ACR postulate that biopsy can sometimes be useful in diagnosing metastatic disease.

DISCUSSION

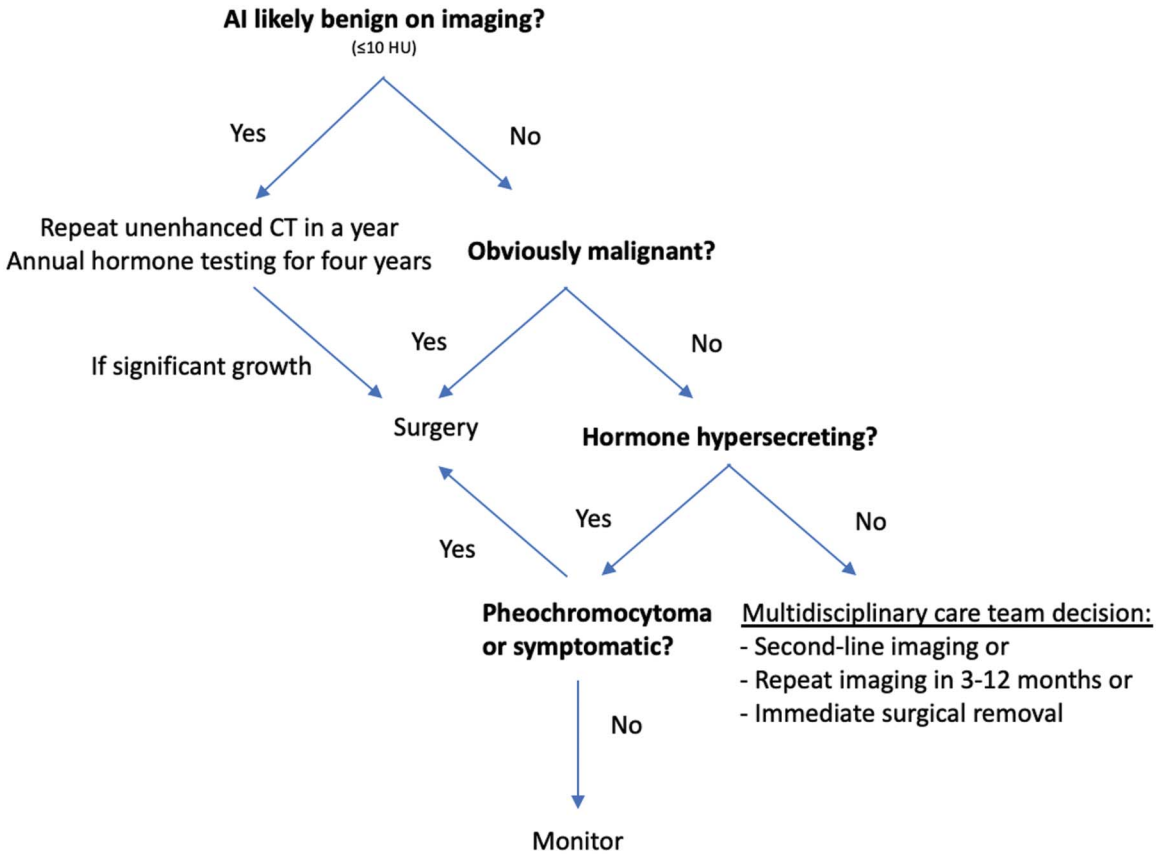
In reviewing the most recently published guidelines of the major fields involved in treating AIs—endocrinology, endocrine surgery, urology and radiology—there are many points of convergence (see Appendix). In fact, there is little debate as to the best initial workup of an AI; rather, the most significant controversy is regarding the management of masses that appear indeterminate on CT and what the appropriate timeline is for repeat imaging and hormonal screening. We have herein reviewed and summarized the recommendations from ESE, CUA, AACE/AAES, ACR and KES (see Appendix). In the following discussion we provide our recommendations, when appropriate, on how to best manage the cases in which the guidelines differ based on current literature and our experience as a multidisciplinary team at a large academic institution with a high volume of adrenal disease (see figure).

In accordance with all reviewed guidelines we recommend that every patient with an AI should receive an unenhanced CT if they have not had one already. The AI on the initial CT should be assessed as benign or indeterminate based on lesion density (10 HU or less) and diameter (greater than 4 cm) respectively. The 4 cm cutoff size is based on retrospective studies demonstrating that the majority of surgically resected ACCs and pheochromocytomas had diameters larger than 4 cm at their time of presentation.[6,7] A recent, large epidemiological study supports the existing literature that the majority of adrenal incidentalomas are in fact nonfunctioning adenomas.[8] At a cutoff of 10 HU the sensitivity of unenhanced CT in predicting an adenoma is around 71% and the specificity is 98%.[9,10] Given the high incidence of adenoma and the high specificity of CT in identifying adenoma, unenhanced CT is an adequate first line screening test.

If the lesion is obviously malignant on CT with features such as large size (greater than 4 cm), heterogeneity and evidence of invasion or necrosis,[11] and the patient is healthy enough to undergo an operation, the patient should be scheduled for surgery. Data from the National Cancer Institute have demonstrated a highly significant difference in recurrence rates and carcinomatosis when ACCs are managed with minimally invasive approaches.[12] Laparoscopic adrenalectomy has historically been considered the gold standard[13] and continues to be an option for small and minimally invasive tumors but, as previously mentioned, open adrenalectomy is the better approach for large and more invasive tumors.[14,15] Additionally there are data to suggest that minimally invasive adrenalectomies for ACC lead to higher rates of peritoneal dissemination.[16] Therefore, we strongly recommend an open approach when treating masses larger than 5 cm, which are consistent with ACC.

In addition to imaging, every patient with a newly diagnosed AI should receive hormonal screening, including a 1 mg dexamethasone suppression test and plasma-free and/or urinary fractionated metanephrine levels. If the patient has hypertension, a renin/aldosterone level should also be drawn. If a pheochromocytoma is diagnosed, it should be surgically resected due to risk of metastasis and uncontrolled hypertension.[17] Medical management prior to surgery is imperative. AACE/AAES recommends 1 to 3 weeks of preoperative α-adrenergic blockade, most commonly with phenoxybenzamine, although doxazosin can be used as well.[3] There are some data to suggest that the addition of metirosine to phenoxybenzamine improves intraoperative hemodynamic stability. Preoperative β-blockade may be indicated if tachycardia or arrythmias persist after maximal α-antagonism.[3] Intraoperatively an arterial line is placed to track blood pressure changes instantaneously with concern for hypertension early in the surgery and significant hypotension after tumor removal. The rate of pheochromocytoma recurrence ranges from around 6.5% to 16.5%, and recurrence rates seem to correlate with size of initial tumor, presence of extra-adrenal disease and association with genetic sydromes.[18,19] In fact, in patients who have hereditary forms of pheochromocytoma recurrence rates are estimated at around 10% in the original adrenal gland and up to 30% in the contralateral gland.[19] The significant risk of recurrence necessitates lifelong monitoring for these patients.

Hormone screening is valuable in cases suspected of both benign and malignant disease. ACC is frequently hormone producing and around 50% of ACCs secrete cortisol specifically, which can be used



Flowchart with authors' recommendations of proposed modifications to existing guidelines in diagnosing and managing adrenal incidentalomas.

as both a prognostic factor and tumor marker.[20] In fact, subclinical Cushing syndrome is the most common hormonal dysfunction caused by AIs.[8] This is usually defined as abnormal dexamethasone suppression screening results, without overt signs or symptoms of cortisol excess, and variable confirmatory testing with other measurements of cortisol production. In the case of abnormal dexamethasone suppression testing without other evidence for cortisol excess patient preference and severity of comorbidities should be taken into account for shared decision making on surgery vs conservative management. There is still controversy related to the relationship between apparently asymptomatic hypercortisolism and diabetes, obesity, dyslipidemia and hypertension.[21]

There is not enough evidence at this time to indicate the single best management of subclinical Cushing syndrome, since progression to frank Cushing syndrome is rare and overall morbidity and mortality due to this condition are unknown. In patients with true Cushing syndrome scheduled for adenoma resection preoperative care must include management of comorbid conditions such as diabetes and hypertension, and intraoperative planning includes special attention to prophylactic antibiotics and stress dosing cortisol.[3] If the mass is indeterminate or suspected to be ACC or if the patient has clinical signs and symptoms of feminization/virilization, we recommend testing for sex steroids and steroid precursors. ACCs are much more likely to secrete steroids than adenomas, with around 40% of ACCs secreting androgens or estrogen,[20] and measuring urinary steroid levels can help differentiate between benign and malignant disease in patients with indeterminate imaging.[22]

If an AI is likely an adenoma and found to be aldosterone secreting, it should be managed with mineralocorticoid receptor antagonists or surgery, as excess aldosterone is an independent risk factor for cardiac disease.[3,23] For patients healthy enough to undergo surgery who have imaging and AVS findings suggestive of a benign aldosterone secreting adenoma, laparoscopic adrenalectomy is the treatment of choice.[3] Preoperative potassium repletion is imperative, and most patients will receive preoperative mineralocorticoid receptor antagonist therapy. For patients who cannot or refuse to undergo surgical management or are suspected of idiopathic adrenal hyperplasia based on AVS, medical management with spironolactone or eplerenone is preferred.[3] If the mass is characterized as benign on

imaging and nonfunctional on hormone assay, such as an adrenal myelolipoma, no operative management should be offered.

In a patient with history of malignancy a newly discovered AI is suspicious for metastasis. It is estimated that 75% of asymptomatic AIs in patients with cancer are due to metastasis,[15] and the most common carcinomas that metastasize to the adrenal glands are from the kidney, lung, breast, gastrointestinal tract and malignant melanoma.[24] If the mass is likely metastatic disease, for example in the setting of a patient with a history of extra-adrenal malignancy and an indicative PET, metastasectomy may be considered. In the case of nonsmall cell lung carcinoma adrenal metastasectomy resulted in low rates of complication and led to a durable 5-year overall survival of 25%.[25] Adrenalectomy may confer a survival benefit to patients with metastatic melanoma, especially in cases where metastasis is limited to the adrenal gland.[26] Additionally there are data to suggest that adrenalectomy for metastatic renal cell carcinoma has the ability to prolong lifespan in select patients with low rates of complications.[27] In patients who are suitable surgical candidates with metastatic disease confined to the adrenal gland adrenal metastasectomy should be considered.

If the mass appears to be benign, there is controversy over whether it should be reimaged in the future. AACE/AAES provide the most conservative guidelines and recommend imaging at 3 to 6 months, citing the rate at which seemingly benign AIs can transform.[3] The risk of enlargement is 6% after 1 year, 14% after 2 years and 29% after 5 years.[28] A limitation with this study is the masses included in it are not classified as benign vs indeterminant on CT, and hormonally functional masses are included in the data set. The ESE recommends no further followup, citing followup studies including 2,300 patients in which no initially benign appearing AIs became malignant.[1] The risk of malignant transformation of a benign appearing adrenal mass appears to be the same as the risk of developing cancer from the amount of radiation in CT. Specifically it is estimated that less than 5% of AIs are malignant and that less than 1% of initially benign appearing and nonfunctional AIs develop malignancy.[29] The ACR also recommends no further followup. Given the conflicting data on the frequency of masses that initially appear benign but later show malignant potential, we recommend a single followup scan in 12 months. The growth rates of benign AIs, including cortisol producing masses, are estimated to be low with a low to nonexistent rate of malignant transformation. Collienne et al reported rates of growth of 0.35 mm per year for apparently nonfunctioning adenomas and 0.53 mm per year for cortisol secreting masses, and none of the masses in their population of 93 patients developed malignant transformation.[30] In a large retrospective study Tasaki et al reported that only 8.6% of their patients had mass growth increases greater than 1.0 cm during followup and, despite this growth, these masses were confirmed as benign on pathology.[31] The only malignancies in their study were discovered on initial imaging and subsequently resected.

Given the literature reporting the majority of AIs have growth rates less than 1.0 cm a year and the risk of malignant transformation of benign appearing lesions is 0% to less than 1%,[29–31] we do not believe there is justification for earlier routine repeat imaging for masses that are likely benign according to radiologist determination. If there are any radiological features more concerning for an indeterminate lesion, further workup should be initiated as described later in this discussion. Furthermore, we believe the risk of missing a malignant lesion is great enough to justify the additional radiation of a followup CT and that, based on the evidence above, 12 months is long enough to gauge the stability of the mass. If the mass has changed significantly in size or homogeneity, further workup should be initiated.

There is also debate as to the utility of repeat hormone testing. The ESE recommends against it while the other organizations advocate for annual testing for 4 to 5 years. ESE guidelines postulate that the rate of asymptomatic hormonal secretion is low and that the most common hypersecretion syndrome is autonomous cortisol secretion, which usually does not warrant intervention.[1,29] AACE/AAES counter this by citing the risk of new onset hormone secretion, which is 17% after 1 year, 29% after 2 years and 47% after 5 years.[28] The KES recommends annual hormonal screening for 5 years only for tumors larger than 3 cm as they have a greater risk of hormone hypersecretion.[5] The question then comes down to whether it is important for the clinician to identify hormonal changes, even if they may have never affected the patient. Given the severity of the complications from hormone excess and the low risk and cost of a blood test, we recommend annual blood testing for 4 to 5 years and a symptom screen at that time as well. Annual blood tests also help ensure that these patients are not lost to followup.

If the AI appears indeterminate on imaging and is nonhormone producing, there is no single recommendation for management. Obtaining second line imaging, repeat imaging in 3 to 12 months and immediate surgery are all considered reasonable options. We recommend shared decision making in a multidisciplinary forum with the patient about their comorbidities, compliance and preference when deciding which option to pursue. If the patient and provider opt for repeat imaging, they can choose a time frame between 3 and 12 months based on how

concerned the provider is for malignancy on initial imaging. If repeat imaging shows significant growth, the provider should recommend resection at that time.

Regarding second line imaging, MRI is most appropriate in high risk populations (including pregnant women and people younger than 40 years old), and PET can be useful in patients with a history of malignancy. CT with washout is the appropriate second line imaging for establishing a diagnosis. Biopsy is of limited value and should only be pursued when suspicion of primary adrenal malignancy is remote, given the risk of dissemination, and pathology would directly influence clinical management, such as in the case of likely metastatic disease.

If the patient has bilateral AIs, the clinician should consider screening for congenital adrenal hyperplasia with 17-hydroxyprogesterone. If the bilateral AIs are likely to be metastasis from a known other malignancy, adrenal function should be assessed. Otherwise, the masses should be investigated as individual AIs. While both KES and ESE guidelines allow for partial adrenalectomy in rare cases of bilateral AIs, such as in bilateral pheochromocytomas in the setting of genetic disease, the risks of recurrence, disease dissemination and adhesion creation limiting chances of future successful resection must be weighed against the oncologic benefits of reduced tumor burden.

The major limitation of this study is that it is a critical review of existing guidelines and therefore does not provide new evidence on how management of AIs affects prognosis. In this discussion the authors have made recommendations on how to manage discrepancies in the guidelines based on the reviewed literature and their experience as academic urologists, urological radiologists and endocrinologists (see figure). This work does not purport to represent new guidelines; rather, the goal of this review is to offer a multidisciplinary institutional perspective and promote continued dialogue on how to manage AIs.

CONCLUSIONS

There is a great deal of overlap between the ESE, CUA, AACE/AAES, ACR and KES guidelines, and best practices likely lie at their confluence. For areas of controversy among the guidelines the physician must work with the patient's multidisciplinary care team, as well as the patient himself or herself, and come to consensus on the best course of action for each individual patient. Future research is needed to help optimize both patient health and health care costs.

Appendix. *Summary of guidelines*

Recommendations	ESE	CUA	AACE/AAES	ACR	KES
First stage of AI workup: Imaging (CT noncon benign features $\leq$10 HU and $<$4 cm in diameter)	x	x	x	x	x
CT with washout as second-line imaging	-	x	x	x	x
Hormone testing at diagnosis	x	x	x	x	x
No surgical management for benign mass	x	x	x	x	x
Reimaging for initially benign appearing mass	no	12 mos	3-6 mos	no	12 mos
Repeat hormonal testing after initial normal panel	no	Annual	Annual	N/A	Annual
Repeat imaging for indeterminate CT	6-12 mos	3-6 mos	N/A	6-12 mos	3-6 mos
Surgery for masses appearing malignant on initial CT	x	x	x	x	x
Resection of cortisol-secreting adenoma on individual basis	x	x	x	N/A	x
Pheochromocytoma must be resected	x	x	x	x	x
Surgery or melanocortin receptor antagonist for Aldosterone-secreting adenomas	N/A	x	x	N/A	x
17-hydroxyprogesterone levels for bilateral AI	x	N/A	N/A	N/A	x
MRI first line for high-risk populations	x	N/A	N/A	N/A	x
PET second line for patients with history of malignancy	x	x	x	x	x
Biopsy of limited value	x	x	x	x	X

Guidelines with different institutional recommendations are in bold.

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