ORIGINAL ARTICLE

Management of Adrenal Incidentalomas: A Survey of Physicians from the Middle East and Africa

Prise en charge des Incidentalomes Surrénaliens : une Enquête chez les Médecins du Moyen Orient et d'Afrique

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Abstract

Introduction: Adrenal incidentaloma (AI) is a common finding from increased imaging use. Several guidelines direct evaluation and management, but limited data exist on real-world practices.
Aim: To describe the knowledge and practices of physicians from the Middle East and Africa (MEA) in AI.
Methods: An online survey evaluated the definition of AI, diagnostic investigations, management approach, and long-term follow-up of patients with AI.
Results: 171 questionnaires were analysed. Adult and pediatric endocrinologists represented 71.4% of participants. A homogenous mass, < 4 cm and < 10HU, was considered benign by 57.9% of the respondents. The threshold of 4 cm for tumor size was considered suggestive of malignity by 64%. A minority, 34 (19.9%), indicated that no further imaging was required if a non-contrast CT scan was consistent with a benign adrenal mass. Most important endocrinopathies would routinely be excluded: hypercortisolism (97.7%), pheochromocytoma (95.3%), and primary hyperaldosteronism (87.1%). In a lesion considered biochemically inactive at the outset, 56.4% of the respondents would have recommended repeated biochemical testing, and 42.8% would have followed up the patients for 4 and 5 years, irrespective of radiological features.
Conclusions: There is an under-appreciation of the risk of malignancy of AI > 4 cm and a tendency of over-investigating patients in whom a benign tumor has been established, with repeated unnecessary biochemical and radiological evaluation, revealing sub-optimal adherence to guidelines regarding AI in this region.

Keywords: adrenal incidentaloma; guidelines; guideline adherence; adrenocortical carcinoma; Cushing syndrome; pheochromocytoma.

Résumé

Introduction : L'incidentalome surrénalien (IS) est devenu fréquent de par l'utilisation accrue des examens d'imagerie. Plusieurs recommandations sont proposées pour sa prise en charge mais les pratiques sont peu connues.
Objectif : Décrire les connaissances et les pratiques des médecins du Moyen-Orient et d'Afrique dans l'évaluation et la prise en charge des IS.
Méthodes : Une enquête en ligne a évalué les connaissances et les pratiques des médecins concernant les investigations, la prise en charge et le suivi des patients ayant un IS.
Résultats : 171 questionnaires ont été analysés, 71,4 % des participants étaient des endocrinologues adultes et pédiatriques. Une masse homogène, <4 cm et de densité <10UH était considérée bénigne par 57,9 % des participants. Le seuil de 4 cm pour la taille était considéré comme un signe de malignité par 64 % des médecins. Une minorité, 34 (19,9 %), a indiqué qu'aucune autre imagerie n'était nécessaire si la tomodensitométrie était en faveur de la bénignité. Les endocrinopathies systématiquement exclues étaient l'hypercortisolisme (97,7 %), le phéochromocytome (95,3 %) et l'hyperaldostéronisme primaire (86,5 %). En cas de lésion considérée au départ comme non sécrétante, 56,4 % des praticiens auraient répété les dosages hormonaux et 42,8% auraient suivi leurs patients pendant 4 à 5 ans, quelles que soient les caractéristiques radiologiques de l'IS.
Conclusions : Il existe une sous-estimation du risque de malignité des IS > 4 cm et une tendance à un excès d'exploration des tumeurs bénignes, révélant une adhésion sous-optimale aux guides pratiques concernant l'IS dans cette région.

Mots clés : incidentalome surrénalien; recommandations; adhésion; corticosurrénalome; syndrome de Cushing ; phéochromocytome.

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LA TUNISIE MEDICALE-2025; Vol 103 (11): 1698-1706 DOI: 10.62438/tunismed.v103i11.5677

Introduction

An adrenal incidentaloma (AI) is an adrenal mass detected on imaging that is not performed for suspected adrenal disease. In most cases, AIs are non-functioning adrenocortical adenomas but may represent conditions requiring a specific intervention and management strategy (1-4).

Several guidelines have been developed to provide clinicians with the best possible evidence-based and cost-effective recommendations for managing patients with AI (5-9). Four crucial clinical questions need to be posed: how to assess the risk of malignancy, how to define and manage low-level autonomous cortisol secretion, who should have surgical treatment and how should it be performed, and what follow-up is required if AI is not surgically removed (5-9).

As there have been updates in the recommendations for the management of AI, new aspects of management and/or surveillance are summarised in the European Society of Endocrinology (ESE) guidelines 2023 (10). These are presented and contrasted with previous guidelines (11). Fundamental recommendations are based on the setting of a benign adrenal adenoma, which is homogenous and exhibits a density < 10 Hounsfield units (HU) on the non-contrast Computed Tomography (CT) and where no further follow-up is required, irrespective of its size. Surgery is recommended for masses > 4 cm, exhibiting > 20 HU on the non-contrast scan, having consulted with a multidisciplinary team. At the same time, an individualized approach and consultation with a multidisciplinary team are recommended for adrenal masses > 4 cm, demonstrating unenhanced 11-20 HU. For intermediate adrenal nodules < 4 cm, with an unenhanced 11-20 HU, immediate additional imaging, followed by follow-up imaging in 12 months with a non-contrast CT or Magnetic Resonance Imaging (MRI), is required. Recommendations exist against repeated hormonal workup after establishing non-functional tumors at initial evaluation unless clinical signs consistent with an endocrinopathy emerge or comorbidities worsen (10).

Earlier on, by contrast, the ESE in 2016 also recommended that in homogenous lesions < 4 cm exhibiting <10 HU on non-contrasted CT scans (5), no further imaging was required. With lesions < 4 cm and exhibiting 11-20 HU, immediate additional imaging with another modality or interval imaging within 6 to 12 months with either a non-contrast CT scan or MRI was recommended. In individuals with lesions > 4 cm and unenhanced > 20 HU, surgery without further delay was required. As for hormonal follow-up of nonfunctioning tumors, it was recommended against repeated hormonal workups unless new clinical signs of endocrine activity appear or worsen (5).

Despite the availability of clinical practice guidelines on the management of AI published by the ESE in 2016 and 2023 (5, 10), we suspect they may be variably implemented. There is a need to determine the degree to which these are implemented for initial evaluation, further management, and subsequent follow-up. Institutional, regional, or national audits, surveys, outcomes, and quality assurance assessments are crucial to enhancing future patient care (12-14). Because most patients are asymptomatic, clinical decision-making largely depends on physician discretion. (15-16).

Exploring the physicians' approaches to management is crucial in gaining insights into the relative adherence to guidelines and standards of care (17-18). It is expected that variations exist in the manner in which physicians adhere to guidelines in regions, for example, the Middle East and Africa (MEA), where many clinicians follow different schools of medical practice, depending on their past experiences and affiliations, a phenomenon we have previously identified relative to other endocrine conditions (19-20). In this study, we aimed to ascertain the practices in diagnosing and managing AI by physicians in relevant hospital specialties from the MEA region using a case-based web-presented survey.

Methods

Target population

In the absence of a single MEA regional endocrine society, without a membership list to define a study targeted population, the target population was identified from a list of electronic mail, pooled from continuous professional development delegates, speakers, authors, or members of various scientific groups or forums from multiple parts of the MEA region. In addition, the group's professional contacts were canvassed as practicing in the target disciplines of interest. Consequently, several questions were added to the survey to delineate the demographic and professional profiles of the respondents, and their practice descriptions were also included as in our previously published surveys (19-21).

Survey Management

A web-based commercial survey management service (SurveyMonkey Inc. San Mateo, California, USA; www.surveymonkey.com) was used. All participants received an initial email or a link, which explained the rationale of the survey and what was required from consenting respondents, followed by three subsequent reminder emails during the study period. Each message included the principal investigator's affiliations and contact details and a unique email-specific electronic link to the questionnaire. The survey website was open for 11 months, from February 1, 2019, to December 31, 2019. Survey responses were collected and stored electronically for anonymous analysis.

Survey Questionnaire

The Supplementary Material (Appendix 1)(is published as supplementary data on the website.) includes the questionnaire. The first part captured the professional and

demographic profiles of the respondents. The AI survey questions were adapted from a previously published survey from Spain (18). This survey incorporated an index case with questions based on it. It included broad aspects of AI management, initial hormonal and radiological evaluation, imaging and hormonal function tests to complete the assessment, surgery indications, and clinical follow-up. All questions were close-ended, multiple choice questions of several types (yes/no, single choice and multiple options, grid and 5 points agreement scales), depending on the issues addressed in each question. The answers were interpreted based on the gold standard approaches recommended by the 2016 and 2023 ESE guidelines, considering the respondents may have yet to read the latest guidelines.

Data analysis

The survey software tools were used to calculate summary statistics for responses to each question. As each participant may not have answered all the questions, the proportion of respondents providing a given answer was calculated individually, using the number of respondents for that question as the denominator. Although we have captured several demographic and clinical features to characterize the study, we have refrained from undertaking any subgroup analysis.

Results

General characteristics of the respondents

Of 467 invitations, 177 participated, and 171 (96.6%) questionnaires that identified the index case as an AI were analysed. Demographic and professional profiles of the respondents are summarised in Table 1. Responses from the Arabian Gulf constituted nearly two-thirds (57.3%) of the studied cohort. Most (78.4%) were established senior physicians, 84.2% had been in clinical practice for more than 11 years, and 63.2% were adult endocrinologists. Most respondents (57.3%) practiced in public service, while most practiced in university and/ or tertiary hospitals (75.4%).

The organization of care for AI

The respondents recommended that patients with an AI should be discussed in a multidisciplinary expert team meeting when there is evidence of significant tumor growth during follow-up imaging (71.0%), when there is evidence of hormone excess (including 'autonomous cortisol secretion') (59.2%), if adrenal surgery was not being considered (14.8%), and if imaging was consistent with a benign lesion (10.7%) (table 2).

Benign versus malignant assessment

When establishing whether an adrenal mass is likely benign or malignant, 114 respondents (66.7%) stated that this was an essential step to determine at initial detection.

Table 1. The demographic and professional profiles of the 171 respondents included in the analysis.

Variables	Details	Number (%)
Origin	Middle East	124 (72.5%)
	North Africa	23 (13.5%)
	Sub-Saharan Africa	24 (14%)
Type of clinical practice	Mostly, public health service	98 (57.3%)
	Mostly private practice	43 (25.1%
	Both	30 (17.5%)
Nature of clinical practice	University or teaching	129 (75.4%)
	District or community	35 (20.5%)
	Other services	7 (4.1%)
Specialties	Adult endocrinology	108 (63.2%)
	Pediatric Endocrinology	14 (8.2%)
	GIM with Endocrine interest	17 (9.9%)
	GIM with Subspecialties	22 (12.9%)
	Other specialties	10 (5.9%)
Career stages	Senior (Consultant/ Attending)	134 (78.4%)
	Mid-Grade (Specialist/ Fellow)	37 (21.6%)
Years in practice	≤10 years	27 (15.8%)
	11-20 years	56 (32.7%)
	21-30 years	58 (33.9%)
	> 30 years	30 (17.6%)
How many patients (new or follow-up) with adrenal mass have you encountered in the last six months	None	37 (21.6%)
	1-5	84 (49.1%)
	6-10	38 (22.2%)
	>10	12 (7.0%)

GIM: General internal medicine

Further, 56 % of respondents considered size the most important factor in determining whether an incidentally found adrenal mass is benign or malignant (Figure 1 Upper), and 64% considered 4 cm as the threshold size for malignancy risk (Figure 1 Lower). Aside from size, other features were considered in suspecting malignancy, including the shape of the mass (85.2%), the attenuation coefficient or density in HU (79.3%), and the rapidity of contrast media washout on enhanced CT (66.9%) (table 2). Additionally, the texture or homogeneity of the mass (55.6%) and laterality (unilateral versus bilateral) (31.8%) were also considered relevant factors. Besides, 84 (49.1%) thought a homogeneous and lipid-rich mass is very likely benign, 99 (57.9%) considered that an AI which is homogeneous, smaller than 4 cm, and HU ≤ 10 on non-contrast CT is consistent with a benign adrenal mass and 34 (19.9%) indicated that if a non-contrast CT is consistent with a benign adrenal mass, then no further imaging is required (Table 2). For indeterminate adrenal masses on non-contrast CT without hormone excess, the preferred management options included interval imaging in 6–12 months, using non-contrast CT or MRI (69.4%), immediate additional imaging with another modality (29.4%), adrenal biopsy (10.0%), and surgery without further delay (4.1%) (Table 2). When further imaging is needed to clarify the diagnosis of AI, MRI was preferred by 53.5% of respondents, followed by CT (34.1%) (Table 2).

Table 2. Clinical and radiological assessment of the malignant potential of an adrenal incidentaloma*

Questions	Responses	Number (%)
A. It is recommended that patients with AI be discussed in a multidisciplinary expert team meeting (N=169)	A. When evidence of significant tumor growth during follow-up imaging.	120 (71.0%)
	B. When there is evidence of hormone excess (including autonomous cortisol secretion)	100 (59.2%)
	C. If adrenal surgery is NOT considered.	25 (14.8%)
	D. If imaging is consistent with a benign lesion.	18 (10.7%)
B. To establish if an adrenal mass is benign or malignant (N =171)	A. An attempt to establish this is recommended during initial detection.	114 (66.7%)
	B. Hounsfield units ≤10, homogeneous and smaller than 4 cm, on non-contrast CT, is consistent with a benign adrenal mass.	99 (57.9%)
	C. A homogeneous and lipid-rich mass is very likely benign.	84 (49.1%)
	D. No further imaging is required if the non-contrast CT is consistent with a benign adrenal mass.	34 (19.9%)
C. What other aspects, besides size, do you consider important to suspect malignancy? Check all that apply (N=169)	A. shape of the mass (irregular vs. regular; unclear vs. clear margins).	144 (85.2%)
	B. The attenuation coefficient (density) [in Hounsfield units]	134 (79.3%)
	C. The washing time (Rapidity of washout of contrast media on enhanced CT).	113 (66.9%)
	D. Texture (homogeneity).	94 (55.6%)
	E. Laterality (unilateral versus bilateral).	53 (31.4%)
D. If the adrenal mass is indeterminate on non-contrast CT and the results of the hormonal workup do not indicate significant hormone excess, options considered by a multidisciplinary team acknowledging the patient's clinical context include (N=170).	A. Interval imaging in 6–12 months (non-contrast CT or MRI)	118 (69.4%)
	B. Immediate additional imaging with another modality	50 (29.4%)
	C. Adrenal biopsy for cytological/histological confirmation.	17 (10.0%)
	D. Surgery without further delay.	7 (4.1%)
E. For AI, if further imaging is needed to clarify the diagnosis, what imaging modality would you use? One choice is possible (N=170).	A. Computed Tomography (CT)	58 (34.1%)
	B. Magnetic Resonance Imaging (MRI)	91 (53.5%)
	C. Other	21 (12.4%)

*Complementary information is provided in Figure 1. **AI**: adrenal incidentaloma

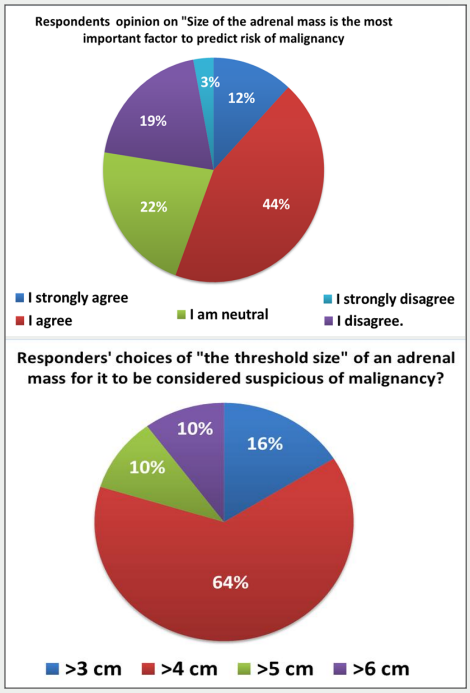

Figure 1. The respondents' views on the value of the size of an adrenal incidentaloma in predicting malignancy (Upper Panel) and the threshold size of the adrenal mass to be considered suspicious of malignancy (Lower Panel). The size of an adrenal mass is a very important predictor for malignancy and a threshold of more than 4 cm, especially if there are malignant features. Notably, the ESE 2023, a homogenous mass <4 cm with HU <10, requires no follow-up.

Endocrine investigations of patients with AI

Respondents' approaches and choices of endocrine screening modalities for patients with AI are shown in Table 3. Most (98.2%) concurred that evaluating excess hormone production is critical before considering surgical intervention for an AI. In decreasing order, investigations were implemented to check for hypercortisolism (97.7%), pheochromocytoma (95.3%), and primary hyperaldosteronism (86.5%) (Table 3). To screen for possible hypercortisolism (Cushing's Syndrome), both overnight (1 mg) dexamethasone suppression test (DST) and 24-hour urinary-free cortisol would have been requested by half of the respondents (50.9%) (Table 3). Most (79.4%) would have employed 24-hour urinary fractionated metanephrines and catecholamines to screen for pheochromocytoma. Concerning the evaluation of primary aldosteronism in normotensive individuals, 72 respondents (42.4%) preferred using the combination of plasma aldosterone to renin ratio (ARR) and serum potassium. In comparison, 56 respondents (32.9%) preferred ARR in isolation, whereas 42 respondents (24.7%) indicated serum potassium as the screening test. In hypertensive individuals, 103 respondents (60.2%) favored using ARR and serum potassium. In comparison, 62 respondents (36.3%) indicated they would rely on the plasma ARR alone. Confirmatory tests for suspected primary hyperaldosteronism in subjects with an AI

included 80 respondents (47.3%) who endorsed the saline overload test. A combination of the saline and fludrocortisone suppression tests was preferred by 25 respondents (14.8%) (Table 3).

Table 3. Respondents' endocrine investigations of adrenal incidentaloma

Questions	Responses	Number (%)
A. Do you agree with the statement: «Before any surgical exploration of an AI is contemplated, it is essential to carry out some investigations to screen for excess hormone production.» (N=171)	A. I strongly agree.	148 (86.5%)
	B. I agree.	20 (11.7%)
	C. I am neutral.	1 (0.6%)
	D. I disagree.	2 (1.2%)
	E. I strongly disagree.	0 (0.0%)
B. In an AI, diagnostic evaluations aim to screen for the following: Check all that apply. (N=171)	A. Hypercortisolism.	167 (97.7%)
	B. Pheochromocytoma.	163 (95.3%)
	C. Primary hyperaldosteronism.	148 (86.5%)
	D. Sex-hormone-producing tumor.	82 (48.0%)
	E. Congenital adrenal hyperplasia.	48 (28.1%)
	F. Other hormone secretion.	22 (12.9%)
C. Which test would you use to **screen** for possible hypercortisolism (Cushing syndrome)? Only one choice is possible? (N=171)	A. Overnight (1 mg) DST only	59 (34.5%)
	B. 24-hour UFC only	19 (11.1%)
	C. High-dose DST	6 (3.5%)
	D. Both A+B	87 (50.9%)
D. Which test would you use to screen for possible pheochromocytoma in a subject with an AI? Check all that apply (N=170)	A. 24-hour urinary fractionated metanephrines catecholamines	135 (79.4%)
	B. plasma free metanephrines.	82 (48.2%)
	C. Plasma free catecholamines.	28 (16.5%)
A. Which test would you use to screen for possible primary hyperaldosteronism in a normotensive individual with an AI? One choice only is possible (N=170)	A. Serum potassium.	42 (24.7%)
	B. Aldosterone to Renin ratio.	56 (32.9%)
	C. Both tests	72 (42.4%)
B. Which test would you use to screen for possible primary hyperaldosteronism in a hypertensive individual with an AI? One choice only is possible (N=171)	A. Serum potassium.	1 (0.6%)
	B. Aldosterone to Renin ratio	62 (36.3%)
	C. Other tests	5 (2.9%)
	D. Both A+B	103 (60.2%)
C. What test would you use if further tests are required to confirm suspected primary hyperaldosteronism in a subject with an AI? One choice only is possible (N=169)	A. Saline overload test.	80 (47.3%)
	B. Fludrocortisone suppression test	16 (9.5%)
	C. Captopril test	9 (5.3%)
	D. Both A + B	25 (14.8%)
	E. Other tests.	7 (4.1%)

AI: adrenal incidentaloma; **DST**: Dexamethasone suppression test, **UFC**: urinary-free cortisol

Surgical resection and clinical surveillance of AI

Figure 2 shows the referral practices for surgical resection of an AI based exclusively on the size of the mass (Figure 2 Upper) or the final diagnosis (Figure 2 Lower).

The respondents' choices of clinical surveillance strategies when surgery was not deemed to be initially indicated are shown in Table 4. Most respondents (79.8%) preferred a combined approach of imaging tests and biochemical investigations for monitoring an AI. Computed tomography was the preferred choice by 70.6%. There was an obvious dichotomy in respondents' recommendations concerning either repeating or not repeating endocrine biochemical investigations in a previously fully investigated adrenal incidentaloma < 4 cm in size at the outset (Yes: 57.4% vs. No: 42.6%; respectively). During long-term surveillance, specifically biochemical evaluation of an adrenal incidentaloma, respondents would have focused on excluding hypercortisolism (92.5%), pheochromocytoma (87.0%), and primary hyperaldosteronism (75.8%).

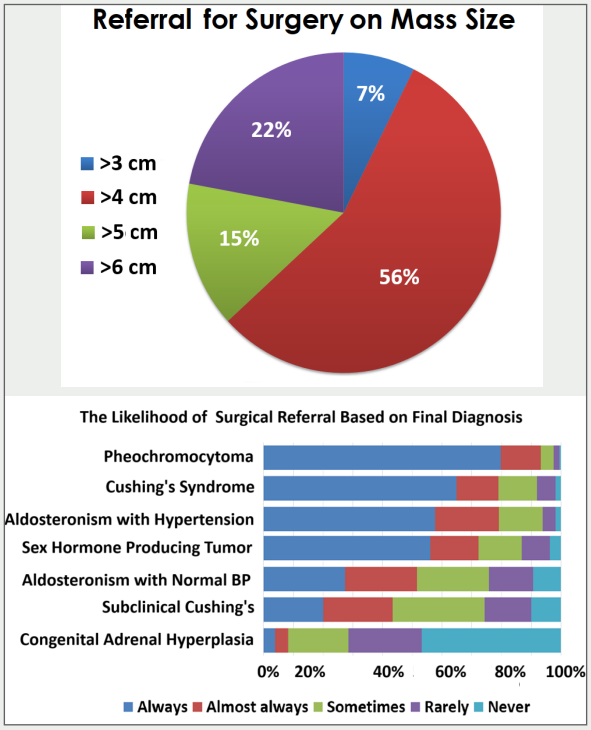

Figure 2. The proportion of respondents by referral of an adrenal incidentaloma for surgical resection based solely on the mass size with a cut off of 4 cm by 56% of respondents (Upper Panel) or based on the final diagnosis predominantly pheochromocytoma, Cushing and Conn's syndrome with poorly controlled BP as the three leading causes.

Responses from Key Subgroups

We refrained from making detailed subgroup analyses based on sample size limitations. However, to enhance the richness of the findings, non-inferential descriptive data across key subgroups are provided in Supplementary Material Table 2 (is published as supplementary data on the website) (including endocrinologists vs. generalists; Middle East vs. North Africa). A few trends of differences between the subgroups are shown. For instance, African respondents were more keen on discussing in a multidisciplinary meeting and establishing a diagnosis for all AI at the outset than Middle Eastern respondents.

Table 4. Respondents' choices of clinical surveillance strategies (if any) of the adrenal incidentaloma when surgery was not deemed to be needed initially

Questions	Options	Responses
A. Please specify the choice of clinical surveillance (if any) of an AI. Only one choice is possible (N=163)	A. Biochemical investigations to assess the evolution of hormone overproduction	10 (6.1%)
	B. Imaging tests to evaluate tumor growth.	23 (14.0%)
	A. Both A+B	130 (79.8%)
	D. None	0 (0%)
B. Please specify the choice of imaging modality of the AI. Only one choice is possible. (N=163)	A. Computed tomography scanning	115 (70.6%)
	B. Magnetic Resonance Imaging	48 (29.4%)
C. Would you keep repeating endocrine biochemical investigations in a previously fully investigated adrenal incidentaloma < 4 cm in size at the outset? (N=162)	A. Yes	93 (57.4%)
	B. No	69 (42.6%)
D. During the long-term surveillance of an AI, biochemical evaluations will include looking for the following (N=161)	A. Hypercortisolism.	149 (92.5%)
	B. Pheochromocytoma.	140 (87.0%)
	C. Primary hyperaldosteronism.	122 (75.8%)
	D. Sex-hormone excess.	68 (42.2%)
	E. Congenital adrenal hyperplasia.	22 (13.7%)
E. Please specify the active follow-up duration for patients with an AI who did not have surgery. Only one choice is possible. (N=161)	A. up to 3 years	35 (21.7%)
	B. up to 4 years	11 (6.8%)
	C. up to 5 years	58 (36.0%)
	D. up to 6 years	8 (5.0%)
	E. 6 -10 years	49 (30.4%)
F. In patients with an adrenal mass <4 cm with clear benign features on imaging studies (N=163)	A. No further imaging for follow-up is needed in most cases.	46 (28.2%)
	B. Regular imaging for follow-up is required at 12-month intervals.	86 (52.8%)
	C. Further imaging for follow-up is required at 6 months intervals	31 (19.0%)
G. In patients with an «indeterminate» adrenal mass (by imaging) opting not to undergo adrenalectomy following the initial assessment: (N=163)	A. Repeat non-contrast CT or MRI after 6–12 months to exclude significant growth is recommended.	90 (55.2%)
	B. Surgical resection is recommended if the lesion enlarges by more than 20% (in addition to at least a 5 mm increase in maximum diameter) during this period	48 (29.4%)
	C. If the lesion grows below the above threshold, additional imaging should be performed after 6–12 months.	25 (15.3%)
H. Regarding repeat hormonal workup in patients opting not to undergo adrenalectomy following the initial assessment (N=163)	A. Repeated hormonal workup is needed in all patients with AI, even if the hormonal workup at initial evaluation was normal.	66 (40.5%)
	B. Repeated hormonal workup in patients with a normal hormonal workup at initial evaluation is not normally recommended.	22 (13.5%)
	C. For Repeated hormonal workup is recommended for Patients with normal hormonal workup at initial evaluation if new clinical signs of endocrine activity appear.	91 (55.8%)
	D. For Patients with normal hormonal workup at initial evaluation, repeated hormonal workup is recommended if there is an unexplained worsening of comorbidities (e.g., hypertension and type 2 diabetes).	75 (46.0%)
In patients with 'autonomous cortisol secretion' without signs of overt Cushing's syndrome (i.e., Subclinical Cushing's Syndrome)	Patients should be offered surgery as soon as possible (or convenient).	59 (36.4%)
	Annual clinical reassessment is suggested for cortisol excess comorbidities potentially related to cortisol excess	60 (37%)
	The potential benefit of surgery should be considered.	74 (45.7%)

AI: Adrenal incidentaloma

Discussion

Findings from our survey raised several points regarding managing AI, particularly relative to adherence to established guidelines. Fewer than half of the respondents recognized homogenous and lipid-rich lesions as likely benign, and only 57.9% considered that a homogeneous tumor smaller than 4 cm exhibiting less than 10 HU on a non-contrast CT scan was also benign. Of great concern is that only 19.9% indicated that no further imaging is required for a benign adrenal mass. Only 64% of respondents thought that the potential for risk of malignancy exists in lesions > 4 cm. For lesions with indeterminate malignancy potential on CT scan, repeat imaging at 6-12 month intervals was deemed appropriate in two-thirds of respondents. More than half

of respondents would have repeated biochemical testing in individuals whose incidentaloma was previously fully investigated and found non-secretory. These data indicate poor adherence to guidelines for analyzing and managing AI and a tendency for over-investigation.

In this study, we described practice patterns for evaluating and following up AI based on the responses of a convenience sample. This study is the first study from the MEA region and the second worldwide. We adopted a detailed survey instrument in a previously published Spanish study (18). Our sample size was larger than the Spanish one (171 versus 33), and 63.2% were adult endocrinologists, expecting that this group of specialists was likely to adhere closely to published guidelines. Similarities included a high proportion who indicated that the tumor size > 4 cm portended malignancy, and a similar proportion stated the need for an MRI. Notably, in both studies, there was a tendency to repeat biochemical investigations for hormone excess, even in the case of initial normal investigations, despite guidelines suggesting that this was unnecessary (10, 11). We have refrained from undertaking any subgroup analysis limited by the small sample and the multiple interrelated factors.

The implications of relatively few respondents indicating that a lipid-rich adenoma < 4 cm was likely benign and lesions < 4 cm in size and exhibiting less than 10 HU are also benign are far-reaching. These lesions could be falsely misconstrued as malignant, and patients could be inadvertently subjected to expensive investigations, which could generate unnecessary anxiety among patients (22). Over half (56%) of respondents in our study considered tumor size as the most important factor suggesting malignancy in the initial evaluation of AI, and lesions > 4 cm could harbor malignancy for 64%. Our findings are closely aligned with the aforementioned Spanish study (18). By implication, this would indicate that nearly a quarter of respondents, despite being endocrinologists, failed to appreciate that an adrenal mass exceeding 4 cm may harbor malignant potential. The most serious adverse outcome is a delayed cancer diagnosis. Half of the respondents (56%) would have referred AI for surgical treatment starting from 4 cm, and 22% would have referred tumors starting from 6 cm, suggesting a variable threshold for referral for surgery.

In cases of indeterminate masses, it is suggested that additional imaging be performed immediately, and if the tumor is still considered indeterminate and surgery is not performed, interval imaging in 6-12 months is recommended (10). However, in the present study, the respondents were more likely to perform interval imaging in 6-12 months (69.4%), while immediate additional imaging with another modality was indicated in 29.4%. The imaging study to be considered the final arbiter was MRI in 53.5% of respondents. It was impossible to undertake statistical correlations between deviations in practice and the impact on patient's health, primarily as it is a survey of how physicians would respond to specific clinical scenarios. As a rule, Incidentalomas do not undergo malignant transformation over time if originally deemed benign, but the risk is primarily over-investigation and incumbent costs. Our geographical area of interest covers a large heterogeneous area, making complex cost comparisons.

Almost all physicians would invariably perform screening for hypercortisolism and pheochromocytoma in AI. Other assessments conducted in AI included investigation for primary hyperaldosteronism in 86.5% of respondents, exclusion of a sex hormone-producing tumor (48%), and congenital adrenal hyperplasia in 28.1%. Half of the respondents would have requested an overnight (1mg) dexamethasone test and 24-hour urinary-free cortisol for the screening of hypercortisolism. However, only an overnight test is recommended (10). Regarding hormonal function, patients with pheochromocytoma, Cushing's Syndrome, primary hyperaldosteronism with poorly controlled blood pressure, or sex hormone-producing tumors would have been more frequently referred for surgery than being reliant on medical therapy alone.

When there was no indication for surgery, the surveillance proposed by most respondents (79.9%) was both imaging and hormonal re-evaluation. According to the last recommendation, no further imaging is required if the AI is an adenoma (10). In the same way, if the AI was non-secretory at initial evaluation, additional hormonal tests are indicated only if new clinical signs of endocrine activity emerge or if there is a worsening of comorbidities such as diabetes or hypertension. Young people predominate the population of the MENA region. There is remarkable progress in providing basic access to healthcare services, with populations receiving comprehensive health coverage either free or at highly subsidized rates. All available evidence indicates significant improvements in key health indicators. There is considerable pressure on health services due to rising public expectations. [23] There is also a culture of overly defensive medicine in this region and fearing complaints, which may have contributed to the tendency to over-investigate patients. [24]

Determining relevant physicians' practices offers good insight into their management of AI. As a substantial proportion of respondents were endocrinologists, this study provides insight into the practices of specialists expected to be closely aligned with guideline recommendations. However, our study identified clear deviations from the guidelines. [5-10] Published guidelines define accepted initial evaluation, referral, and follow-up recommendations for AI [5-10]. However, the extent of adherence to these guidelines and barriers to appropriate follow-up need to be documented and better understood. [11-12] A correlation between years or type of practice and the likelihood of over-investigating patients may imply a lack of updates in this area. However, we have refrained from any subgroup analysis as several confounders may exist.

Guidelines are designed to provide cost-effective and efficient management of sometimes complex disorders.

One of the greatest potential barriers to adopting guideline strategies is physicians' willingness to embrace changes. Although doctors know the guidelines, they must be more familiar with the recommendations (25). Several strategies have been associated with implementing guidelines, including providing educational material, educational meetings, reminders, auditing and feedback, updates at academic conferences, and continuing professional development symposia at a regional level through relevant professional and educational institutions inter alia of endocrinologists (26). Unfortunately, we did not determine the reasons for non-adherence to scientific society recommendations, particularly the last update in this area and lack of training. However, retrospectively, we evaluated the correlation between years of practice and the likelihood of over-investigation of patients.

With the increasing prevalence of AI and patient workload, guidance should consider cost-effectiveness and safety in managing these cases effectively. Unjustifiably extensive or too frequent investigations may be overly costly to health systems, particularly in resource-limited low and middle-income countries. We have refrained from making detailed calculations of the cost implications of excessive investigation elicited by this study since these may vary across different regions of the MEA. Two previous studies have addressed cost and suggested approaches for prioritization and effective investigations and management using various methods (27, 28). We acknowledge that an in-depth cost analysis, for example, comparing MRI costs in Africa and the Middle East while contextualizing it with the average citizen's income, would have enhanced the study. However, due to regional economic variability, we have intentionally refrained from detailed cost analysis. It is worthwhile pointing out that MRI availability in Africa varies, with, on average, very low density in some regions and predominantly in the private sector.

Several limitations are noteworthy. Firstly, the target population was selected without an established Middle East African endocrine society without a membership list. The target population was identified from a list of electronic mail pulled from continuous professional development (CPD) scientific events. In addition, the group's professional contacts were canvassed as practicing in the target disciplines of interest. We acknowledge that the target sample size was not calculated. Power analysis is needed to determine sample size ideally for calculating statistical analyses and for appropriate generalization to the population. An additional factor of concern is the survey return rate. To answer whether it is generalizable to the population, one has to perform a power analysis to determine the number of completed and usable surveys needed. Respondents from multiple specialty areas, accounting for the observed heterogeneity in responses, skewed in some countries rather than uniform throughout the region as we applied no quotas. In addition, using quality control assessments, survey information relies on what respondents state rather than reflecting their practices (29, 30). The relatively small sample size introduces the potential for either a type I or type II error, further limiting our study. However, our survey is considerably larger (n=171) than the Spanish comparator study in which 33 participants undertook the questionnaire. Doctors may not participate in surveys for several reasons, particularly time constraints, a perception that the questions are irrelevant or poorly designed, lack of benefit from participation, concerns being raised about data privacy, and fatigue from receiving too many requests to participate. Doctors also do not always appreciate the value of participating in surveys. They may also be concerned that it may expose knowledge deficits. Also, the response rate of 37% may be considered sub-optimal, but online surveys can expect to yield a response rate between 25 and 40%. We have used several previously published international surveys to study clinical practice patterns in the MEA, which have provided reliable assessments of diagnostic and treatment trends (19-21). These research endeavors remain, to date, an effective manner to explore physicians' perceptions of an important condition in our region (19-21). One weakness is that the questionnaire was not validated but used previously in the Spanish comparator study, inferring a precedent for its use. Aspects of this survey concerning demographics have been utilized in our multiple studies. [19-21] It could be argued to include open-ended questions where participants could have expressed themselves freely. However, since the options are limited, we list all possible options similar to previous endocrine studies (19-21). However, the previously used questionnaire in Spain may not have been fully adapted to the African and Middle Eastern contexts. However, this is unlikely as the determinants of the responses are mostly clinical. Also, language or clinical culture differences (e.g., Anglophone vs Francophone Africa) may have influenced the understanding or application of guideline terminology.
Furthermore, our survey failed to consider specific contexts in various countries due to language translation and limited numbers. The geographical region in which the survey was conducted represents a number of confounding factors, including economic, social, and cultural differences. Additionally, medical schools of thought in various parts of the globe impart different emphasis with varying degrees of available resources, which influences how screening and treatment differ.

Conclusions

Our survey revealed disparities in clinical practice among physicians in the MEA region regarding managing an AI. This particularly concerned the diagnosis of malignancy and the follow-up modalities. Better adherence to guidelines would improve patient outcomes, reduce unnecessary testing, and ensure more efficient use of healthcare resources, especially in cost-constrained environments. System-related factors (e.g., litigation fears, healthcare access, disrupted continuity of care, and access to records) may contribute to deviation from guideline recommendations. Improvements in

these aspects should mitigate their negative impact on the suboptimal care detected by the survey. Whereas, predictably, endocrinologists provided more concordant responses with the guidelines and were more likely to undertake more specialized dynamic endocrine tests than non-endocrinologists.

Authorship

All the authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship. SAB adapted the questionnaire, managed the online survey, and analysed the data. The rest of the authors reviewed the data and the manuscript for intellectual content.

Conflict of interest

The authors have declared no competing interests.

Funding and sponsorship

No funding was received for this study.

Compliance with ethical principles

The Institutional Review Board of Sheikh Khalifa Medical City, Abu Dhabi, UAE, approved the study. Before participants could access the questions, they provided electronic informed consent.

Data availability statement:

Raw data are available from the corresponding author by a reasonable request

Use of generative artificial intelligence

None

References

1. Sherlock M, Scarsbrook A, Abbas A, Fraser S, Limumpornpetch P, Dineen R, Stewart PM. Adrenal Incidentaloma. Endocr Rev. 2020 41 775-820.
2. Bancos I, Prete A. Approach to the Patient With Adrenal Incidentaloma. J Clin Endocrinol Metab. 2021 106 3331-53.
3. Morelli V, Palmieri S. Adrenal incidentaloma: differential diagnosis and management strategies. Minerva Endocrinol. 2019 44 4-18.
4. He X, Peter PR, Auchus RJ. Approach to the Patient with an Incidental Adrenal Mass. Med Clin North Am. 2021 105 1047-63.
5. Fassnacht M, Arlt W, Bancos I, Dralle H, Newell-Price J, Sahdev A, Tabarin A, Terzolo M, Tsagarakis S, Dekkers OM. Management of adrenal incidentalomas: European Society of Endocrinology Clinical Practice Guideline in collaboration with the European Network for the Study of Adrenal Tumors. Eur J Endocrinol. 2016 175 G1-G34.
6. Farrugia FA, Misiakos E, Martikos G, Tzanetis P, Charalampopoulos A, Zavras N, Sotiropoulos D, Koliakos N. A step by step approach in differential diagnosing of adrenal incidentaloma (epinephroma), (with comments on the new Clinical Practice Guidelines of the European Society of Endocrinology). Rom J Intern Med. 2017 55 188-97.
7. Bednarczuk T, Bolanowski M, Sworczak K, Gornicka B, Cieszanowski A, Otto M, Ambroziak U, Pachucki J, Kubicka E, Babinska A, Koperski L, Januszewicz A, Prejbisz A, Gorska M, Jarzab B, Hubalewska-Dydejczyk A, Glinicki P, Ruchala M, Kasperlik-Zaluska A. Adrenal incidentaloma in adults - management recommendations by the Polish Society of Endocrinology. Endokrynol Pol. 2016 67 234-58.
8. Lee JM, Kim MK, Ko SH, Koh JM, Kim BY, Kim SW, Kim SK, Kim HJ, Ryu OH, Park J, Lim JS, Kim SY, Shong YK, Yoo SJ, Korean Endocrine Society CfCPG. Clinical Guidelines for the Management of Adrenal Incidentaloma. Endocrinol Metab (Seoul). 2017 32 200-18.
9. Araujo-Castro M, Iturregui Guevara M, Calatayud Gutierrez M, Parra Ramirez P, Gracia Gimeno P, Hanzu FA, Lamas Oliveira C. Practical guide on the initial evaluation, follow-up, and treatment of adrenal incidentalomas Adrenal Diseases Group of the Spanish Society of Endocrinology and Nutrition. Endocrinol Diabetes Nutr (Engl Ed). 2020 67 408-19.
10. Fassnacht M, Tsagarakis S, Terzolo M, Tabarin A, Sahdev A, Newell-Price J, Pelsma I, Marina L, Lorenz K, Bancos I, Arlt W, Dekkers OM. European Society of Endocrinology clinical practice guidelines on the management of adrenal incidentalomas, in collaboration with the European Network for the Study of Adrenal Tumors. Eur J Endocrinol. 2023 189 G1-G42.
11. Park SS, Kim JH. Recent Updates on the Management of Adrenal Incidentalomas. Endocrinol Metab (Seoul). 2023 38 373-80.
12. Podbregar A, Kocjan T, Rakusa M, Popovic P, Garbajs M, Goricar K, Janez A, Jensterle M. Natural history of nonfunctioning adrenal incidentalomas: a 10-year longitudinal follow-up study. Endocr Connect. 2021 10 637-45.
13. Ichijo T, Ueshiba H, Nawata H, Yanase T. A nationwide survey of adrenal incidentalomas in Japan: the first report of clinical and epidemiological features. Endocr J. 2020 67 141-52.
14. Feeney T, Talutis S, Janeway M, Sridhar P, Gupta A, Knapp PE, Moses J, McAneny D, Drake FT. Evaluation of incidental adrenal masses at a tertiary referral and trauma center. Surgery. 2020 167 868-75.
15. Cambos S, Tabarin A. Management of adrenal incidentalomas: Working through uncertainty. Best Pract Res Clin Endocrinol Metab. 2020 34 101427.
16. Ceccato F, Barbot M, Scaroni C, Boscaro M. Frequently asked questions and answers (if any) in patients with adrenal incidentaloma. J Endocrinol Invest. 2021 44 2749-63.
17. Voltan G, Boscaro M, Armanini D, Scaroni C, Ceccato F. A multidisciplinary approach to the management of adrenal incidentaloma. Expert Rev Endocrinol Metab. 2021 16 201-12.
18. Moreno-Fernandez J, Garcia-Manzanares A, Sanchez-Covisa MA, Garcia EI. Clinical management of adrenal incidentalomas: results of a survey. Endocrinol Nutr. 2009 56 447-51.
19. Beshyah SA Ali KF. Management of adrenal insufficiency: A survey of perceptions and practices of physicians from the Middle East and North Africa. J Diabetes Endocr Pract. 2021 4 125-30.
20. Mofokeng TRP, Beshyah SA, Mahomed F, Ndlovu KCZ, Ross IL. Significant barriers to diagnosis and management of adrenal insufficiency in Africa. Endocr Connect. 2020 9 445-56.
21. Beshyah SA Khalil AB. Clinical practice patterns in managing thyroid nodules: The first survey from the Middle East and Africa. J Diabetes Endocr Pract 2021 4 167-74.
22. Baiguissova D, Laghi A, Rakhimbekova A, Fakhradiyev I, Mukhamejanova A, Battalova G, Tanabayeva S, Zharmenov S, Saliev T, Kausova G. An economic impact of incorrect referrals for MRI and CT scans: A retrospective analysis. Health Sci Rep. 2023 6 e1102.
23. Katoue MG, Cerda AA, García LY, Jakovljevic M. Healthcare system development in the Middle East and North Africa region: Challenges, endeavors and prospective opportunities. Front Public Health. 2022 December 22;10:1045739. doi: 10.3389/fpubh.2022.1045739.
24. Al Awar S, Ucenic TE, Elbiss H. The practice of defensive medicine among physicians in the United Arab Emirates: A clinician survey. Medicine (Baltimore). 2023 Aug 25;102(34):e34701. doi: 10.1097/MD.0000000000034701.
25. Baiardini I, Braido F, Bonini M, Compalati E, Canonica GW. Why do doctors and patients not follow guidelines? Curr Opin Allergy Clin Immunol. 2009 9 228-33.
26. Annesi CA, Talutis SD, Goldman AL, Childs E, Knapp PE, McAneny D, Drake FT. Point-of-care access to clinical guidelines may improve management of incidental findings in the primary care setting. J Eval Clin Pract. 2023 29 632-8.
27. Pereira VC, Silva SN, Vidal AT, Lins GVE, Barreto JOM. How to improve the dissemination of clinical practice guidelines in the Brazilian Unified Health System? Report of a pilot project. Health Res Policy Syst. 2023 21 22.
28. Pereira VC, Silva SN, Carvalho VKS, Zanghelini F, Barreto JOM. Strategies for the implementation of clinical practice guidelines in public health: an overview of systematic reviews. Health Res Policy Syst. 2022 20 13.
29. Hanna FWF, Issa BG, Lea SC, George C, Golash A, Firn M, Ogunmekan S, Maddock E, Sim J, Xydopoulos G, Fordham R, Fryer AA. Adrenal lesions found incidentally: how to improve clinical and cost-effectiveness. BMJ Open Qual. 2020 9.
30. Dwamena BA, Kloos RT, Fendrick AM, Gross MD, Francis IR, Korobkin MT, Shapiro B. Diagnostic evaluation of the adrenal incidentaloma: decision and cost-effectiveness analyses. J Nucl Med. 1998 39 707-12.