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Más Allá del Tamaño Tumoral: Estratificación del Riesgo Hormonal, Caracterización Preoperatoria y Toma de Decisiones Quirúrgicas de Precisión en Incidentalomas Suprarrenales

Beyond Tumor Size: Hormonal Risk Stratification, Preoperative Imaging, and Precision Surgical Decision-Making in Adrenal Incidentalomas

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Edition 5, Year 3, Number 2, 2026

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IECCMEXICO Review

RESUMEN

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Revista IECCMEXICO

Los incidentalomas suprarrenales representan un desafío diagnóstico cada vez más frecuente debido al uso generalizado de estudios de imagen y a la creciente complejidad de las decisiones endocrinológicas y quirúrgicas. Aunque la mayoría de las masas suprarrenales detectadas incidentalmente son benignas, una proporción clínicamente relevante presenta secreción hormonal autónoma o características radiológicas que requieren estudios adicionales. Esta revisión narrativa tuvo como objetivo analizar e integrar la evidencia científica internacional sobre la evaluación hormonal, la caracterización preoperatoria mediante estudios de imagen y la selección de adrenalectomía mínimamente invasiva, incorporando contribuciones relevantes de investigaciones latinoamericanas. Se desarrolló una síntesis temática estructurada de 20 publicaciones científicas, incluyendo guías clínicas internacionales, ensayos clínicos aleatorizados, estudios observacionales, revisiones sistemáticas y metaanálisis, con el propósito de examinar criterios diagnósticos, indicaciones terapéuticas y resultados perioperatorios. La evidencia revisada destacó la importancia de la evaluación sistemática del cortisol, la detección selectiva del hiperaldosteronismo primario y la exclusión bioquímica del feocromocitoma en los contextos clínicos correspondientes. La caracterización radiológica mediante la atenuación tomográfica sin contraste, la homogeneidad de la lesión, las dimensiones tumorales y la resonancia magnética complementaria constituyó un componente fundamental para la estratificación del riesgo de malignidad. Los ensayos clínicos indicaron que la adrenalectomía puede mejorar determinados parámetros cardiometabólicos en pacientes con secreción autónoma leve de cortisol, aunque los beneficios no fueron uniformes entre los estudios. Las investigaciones quirúrgicas comparativas demostraron resultados perioperatorios favorables con la adrenalectomía laparoscópica y robótica, identificándose en algunos metaanálisis menor sangrado, reducción de la estancia hospitalaria y menos complicaciones con los abordajes robóticos. Sin embargo, la selección quirúrgica depende de la complejidad anatómica, la seguridad oncológica, la experiencia institucional y los recursos sanitarios disponibles. Las investigaciones latinoamericanas aportaron evidencia sobre características metabólicas y manejo quirúrgico, destacando la necesidad de adaptar las recomendaciones internacionales a diferentes entornos asistenciales. En conjunto, el manejo óptimo de los incidentalomas suprarrenales requiere integrar la funcionalidad endocrina, los hallazgos radiológicos y los factores de riesgo individuales para establecer estrategias de vigilancia o intervención quirúrgica personalizadas. Se necesitan investigaciones prospectivas multicéntricas que permitan determinar los resultados a largo plazo, perfeccionar los criterios de selección quirúrgica y fortalecer la evidencia aplicable a los sistemas sanitarios latinoamericanos.

PALABRAS CLAVE

incidentaloma suprarrenal, masa suprarrenal, evaluación hormonal, secreción autónoma leve de cortisol, imagenología suprarrenal, adrenalectomía, cirugía mínimamente invasiva, adrenalectomía laparoscópica, adrenalectomía asistida por robot, estratificación del riesgo de malignidad

ABSTRACT

Adrenal incidentalomas represent an increasingly prevalent diagnostic challenge associated with the widespread use of cross-sectional imaging and the growing complexity of endocrine and surgical decision-making. Although most incidentally detected adrenal masses are benign, a clinically relevant proportion exhibit autonomous hormonal secretion or radiological characteristics requiring further investigation. This narrative review aimed to analyze and integrate current international evidence regarding hormonal assessment, preoperative imaging characterization, and the selection of minimally invasive adrenalectomy, incorporating relevant contributions from Latin American investigations. A structured thematic synthesis of 20 scientific publications, including international clinical guidelines, randomized controlled trials, observational studies, systematic reviews, and meta-analyses, was developed to examine diagnostic criteria, therapeutic indications, and perioperative outcomes. The reviewed evidence identified the importance of systematic cortisol assessment, selective screening for primary aldosteronism, and biochemical exclusion of pheochromocytoma in appropriate clinical settings. Radiological characterization using unenhanced computed tomography attenuation, lesion homogeneity, tumor dimensions, and complementary magnetic resonance imaging emerged as a central component of malignancy risk stratification. Randomized evidence indicated that adrenalectomy may improve selected cardiometabolic outcomes in patients with mild autonomous cortisol secretion,

Edition 5, Year 3, Number 2, 2026

E-ISSN: 3061-8045, P-ISSN: 3061-8517

IECCMEXICO Review

although treatment benefits were not uniform across studies. Comparative surgical investigations demonstrated favorable perioperative outcomes with laparoscopic and robotic-assisted adrenalectomy, with certain meta-analyses reporting lower blood loss, shorter hospitalization, and fewer complications with robotic techniques. Nevertheless, operative selection remains dependent on anatomical complexity, oncological safety, institutional expertise, and healthcare resources. Latin American investigations contributed evidence regarding metabolic characteristics and surgical management, highlighting the importance of adapting international recommendations to different clinical environments. Overall, optimal management of adrenal incidentalomas requires integrating endocrine functionality, radiological findings, and patient-specific risk factors to support individualized surveillance or surgical intervention. Further prospective multicenter research is necessary to establish long-term outcomes, refine surgical selection criteria, and strengthen evidence applicable to Latin American healthcare systems.

KEYWORDS

adrenal incidentaloma, adrenal mass, hormonal evaluation, mild autonomous cortisol secretion, adrenal imaging, adrenalectomy, minimally invasive surgery, laparoscopic adrenalectomy, robotic-assisted adrenalectomy, malignancy risk stratification

INTRODUCCIÓN

Adrenal incidentalomas have become an increasingly relevant clinical challenge due to the widespread use of computed tomography (CT), magnetic resonance imaging (MRI), and other diagnostic imaging techniques. These lesions, identified unexpectedly during examinations performed for unrelated medical conditions, encompass a heterogeneous group of adrenal abnormalities, including nonfunctioning adenomas, hormonally active tumors, pheochromocytomas, metastases, and adrenocortical carcinomas. Although most incidental adrenal masses are benign, their detection requires a systematic assessment to distinguish lesions suitable for conservative management from those requiring surgical intervention. This distinction is particularly important because unnecessary adrenalectomy exposes patients to avoidable perioperative risks, whereas delayed recognition of functional or malignant tumors may result in significant clinical consequences (Fassnacht et al., 2023; Rowe et al., 2023).

The diagnostic approach to adrenal incidentalomas has evolved toward the integration of hormonal assessment, advanced radiological characterization, and individualized risk stratification. Current international recommendations emphasize evaluating autonomous cortisol secretion, investigating primary aldosteronism in patients with hypertension or unexplained hypokalemia, and excluding pheochromocytoma when imaging findings do not establish a typical benign adenoma. Simultaneously, radiological parameters such as unenhanced CT attenuation, lesion homogeneity, tumor dimensions, and MRI signal characteristics contribute to estimating malignancy risk and determining the need for additional investigations. Nevertheless, indeterminate imaging findings and mild autonomous cortisol secretion remain important sources of clinical uncertainty (Fassnacht et al., 2023; Funder et al., 2016; Lenders et al., 2014; Nandra et al., 2020).

The therapeutic management of adrenal incidentalomas has undergone substantial changes following advances in minimally invasive surgery. Laparoscopic adrenalectomy has become an established treatment for appropriately selected adrenal lesions, while robotic-assisted approaches have expanded the technical possibilities for complex anatomical dissections. However, surgical eligibility cannot be determined exclusively by tumor size. Hormonal functionality, radiological suspicion of malignancy, local invasion, surgical expertise, and patient comorbidities must be considered when selecting the operative approach. Evidence comparing laparoscopic and robotic adrenalectomy suggests differences in selected perioperative outcomes, although the clinical advantages of either technique depend on institutional experience and patient characteristics (Yip et al., 2022; Gan et al., 2022; Gan et al., 2025).

Another unresolved issue concerns the management of patients with mild autonomous cortisol secretion, particularly when classical manifestations of Cushing syndrome are absent. Previous investigations have demonstrated associations between cortisol autonomy and cardiometabolic abnormalities, including hypertension, impaired glucose metabolism, and increased cardiovascular risk. Recent randomized studies have further examined whether adrenalectomy provides meaningful improvements compared with conservative management, reinforcing the importance of individualized

Edición 5, Año 3, Número 2, 2026 E-ISSN: 3061-8045, P-ISSN: 3061-8517 Revista IECCMEXICO
Edition 5, Year 3, Number 2, 2026 E-ISSN: 3061-8045, P-ISSN: 3061-8517 IECCMEXICO Review

therapeutic decisions rather than uniform surgical indications (Elhassan et al., 2019; Koh et al., 2024; Ueland et al., 2025).

International evidence has also highlighted the importance of adapting diagnostic and therapeutic strategies to different healthcare settings. Studies conducted in Latin America, particularly in Brazil, Chile, and Argentina, have contributed information regarding clinical presentation, metabolic abnormalities, diagnostic evaluation, and surgical outcomes in patients with adrenal incidentalomas. These findings are relevant because differences in access to endocrine testing, advanced imaging, minimally invasive technology, and specialized multidisciplinary teams may influence clinical decision-making and treatment availability (Vilar et al., 2008; Castillo et al., 2008; Rebelo et al., 2023; Chervin et al., 2007).

Despite substantial progress, important questions remain regarding the optimal integration of hormonal findings, imaging characteristics, and surgical criteria. In particular, uncertainty persists concerning the management of radiologically indeterminate lesions, the selection of patients with mild cortisol autonomy who may benefit from adrenalectomy, and the comparative indications for laparoscopic and robotic procedures. These challenges support the need for a comprehensive evaluation of contemporary evidence that connects endocrine diagnosis with preoperative characterization and surgical planning.

The present narrative review aims to critically examine current evidence regarding the hormonal evaluation, preoperative imaging characterization, and selection of minimally invasive surgical approaches for adrenal incidentalomas. Through a structured thematic synthesis of international clinical guidelines, observational investigations, randomized trials, systematic reviews, and relevant Latin American studies, this article addresses the central question of how endocrine, radiological, and clinical findings can be integrated to optimize individualized management. Particular emphasis is placed on identifying factors that support surgical intervention, recognizing circumstances in which surveillance is appropriate, and examining the clinical considerations that influence the selection of minimally invasive adrenalectomy.

DESARROLLO

Adrenal incidentalomas represent a heterogeneous group of lesions whose clinical management requires the integration of endocrine function, radiological characteristics, oncological risk, and surgical feasibility. Their increasing detection has transformed the diagnostic approach to adrenal disease, shifting clinical attention from the identification of symptomatic tumors toward the evaluation of abnormalities discovered in otherwise unrelated medical investigations. Although most incidental adrenal lesions are benign adrenocortical adenomas, a clinically relevant proportion may demonstrate autonomous hormonal secretion or imaging characteristics that warrant further investigation. Consequently, management decisions should not depend exclusively on tumor dimensions but rather on a comprehensive assessment of biochemical, anatomical, and patient-related variables (Fassnacht et al., 2023; Rowe et al., 2023).

Clinical Significance and Hormonal Evaluation

Hormonal assessment constitutes a fundamental component of the initial evaluation of adrenal incidentalomas. Mild autonomous cortisol secretion (MACS) is particularly relevant because it may occur without the characteristic physical manifestations of overt Cushing syndrome while remaining associated with hypertension, type 2 diabetes mellitus, dyslipidemia, and other cardiometabolic abnormalities. Contemporary recommendations define MACS using a post-dexamethasone serum cortisol concentration exceeding 1.8 µg/dL (50 nmol/L) following the 1-mg overnight dexamethasone suppression test, in patients without overt Cushing syndrome. Interpretation requires consideration of potential confounding factors, confirmation of adrenocorticotropic hormone independence when appropriate, and assessment of associated comorbidities (Fassnacht et al., 2023; Elhassan et al., 2019).

Primary aldosteronism represents another important diagnostic consideration, particularly among patients presenting with hypertension or unexplained hypokalemia. Screening generally involves determining the aldosterone-to-renin ratio, with subsequent interpretation according to medication exposure, potassium concentrations, and clinical context.

Edición 5, Año 3, Número 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 5, Year 3, Number 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Identifying aldosterone excess is essential because unilateral disease may be amenable to surgical treatment, whereas bilateral adrenal hypersecretion generally requires medical management. Importantly, the presence of an adrenal nodule does not independently establish the source of aldosterone production, and adrenal venous sampling may be necessary when determining surgical lateralization (Funder et al., 2016).

Pheochromocytoma must also be considered because failure to recognize catecholamine-producing tumors before surgery may precipitate severe hemodynamic complications. Plasma free metanephrines or urinary fractionated metanephrines are established biochemical investigations, particularly when imaging findings are inconsistent with a typical lipid-rich benign adenoma. Confirmed pheochromocytomas require appropriate preoperative preparation, including alpha-adrenergic blockade and individualized cardiovascular optimization. The integration of biochemical findings with radiological assessment is therefore essential for preventing avoidable perioperative complications (Lenders et al., 2014; Fassnacht et al., 2023).

Radiological Characterization and Malignancy Risk

Cross-sectional imaging plays a central role in differentiating benign adrenal adenomas from potentially malignant lesions. Unenhanced CT is particularly valuable because homogeneous adrenal masses demonstrating attenuation values of 10 Hounsfield units or less are highly suggestive of lipid-rich adenomas. Conversely, heterogeneous lesions, irregular margins, elevated attenuation, or evidence of local invasion require additional evaluation. Tumor size remains relevant, especially when combined with suspicious imaging characteristics, but should not be interpreted as an isolated determinant of malignancy (Schieda & Siegelman, 2017; Fassnacht et al., 2023).

MRI provides complementary information through chemical-shift imaging, which can identify intracellular lipid content in adrenal adenomas. Additional imaging techniques, including contrast-enhanced CT and selected functional imaging modalities, may be useful in specific diagnostic scenarios. Nevertheless, diagnostic accuracy depends on appropriate technique selection and recognition of imaging limitations. Certain lipid-poor adenomas, pheochromocytomas, and malignant lesions may demonstrate overlapping radiological appearances, reinforcing the importance of correlating imaging findings with biochemical results and clinical history (Nandra et al., 2020; Johnson et al., 2009).

Selection of Minimally Invasive Surgical Approaches

The decision to perform adrenalectomy should be based on a multidisciplinary assessment of hormonal functionality, suspected malignancy, anatomical complexity, and patient-specific surgical risk. Minimally invasive adrenalectomy is generally preferred for appropriately selected benign adrenal tumors requiring removal because it is associated with reduced postoperative pain, shorter hospitalization, and faster recovery compared with conventional open surgery. However, suspected invasive adrenocortical carcinoma requires particular caution, as complete oncological resection without tumor rupture remains the principal therapeutic objective (Yip et al., 2022; Castillo et al., 2008).

Laparoscopic adrenalectomy can be performed through transperitoneal or retroperitoneal approaches. The transperitoneal technique provides a relatively spacious operative field and familiar anatomical landmarks, whereas posterior retroperitoneoscopic adrenalectomy allows direct access to the adrenal gland without entering the peritoneal cavity. Surgical selection depends on tumor characteristics, previous abdominal procedures, patient anatomy, and surgeon experience. Robotic-assisted adrenalectomy offers articulated instrumentation and enhanced three-dimensional visualization, although its higher procedural costs and uncertain superiority across routine cases require careful consideration (Gan et al., 2022; Gan et al., 2025).

Individualized Management and International Perspectives

The management of patients with MACS remains an important area of clinical investigation. Evidence suggests that selected patients may experience improvements in blood pressure, glycemic control, or other metabolic parameters following adrenalectomy. Nevertheless, the magnitude of benefit varies, and the decision to operate should consider the severity of cortisol-related comorbidities, age, surgical risk, patient preferences, and the likelihood of achieving meaningful clinical improvement (Koh et al., 2024; Ueland et al., 2025).

Edición 5, Año 3, Número 2, 2026
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Revista IECCMEXICO
Edition 5, Year 3, Number 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 5, Año 3, Número 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 5, Year 3, Number 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Studies from Latin America have contributed valuable observations regarding the metabolic characteristics of adrenal incidentalomas, diagnostic practices, and surgical outcomes. Brazilian investigations have highlighted associations between adrenal lesions and cardiometabolic abnormalities, while Chilean surgical experience has contributed evidence concerning laparoscopic adrenalectomy and the influence of tumor size on operative management. These findings support the applicability of internationally recognized diagnostic principles while emphasizing the importance of adapting clinical pathways to regional healthcare resources and institutional expertise (Vilar et al., 2008; Ribeiro Cavalari et al., 2018; Rebelo et al., 2023; Castillo et al., 2008).

OBJETIVO GENERAL Y OBJETIVOS ESPECÍFICOS

General Objective

To critically analyze and integrate current international scientific evidence regarding hormonal evaluation, preoperative radiological characterization, and selection criteria for minimally invasive adrenalectomy in patients with adrenal incidentalomas, with the purpose of establishing a comprehensive, evidence-based framework that supports accurate diagnostic stratification, individualized therapeutic decision-making, and the optimization of surgical outcomes across diverse healthcare settings, including Latin America.

Specific Objectives

Cognitive Domain

- **Identify and describe** the principal epidemiological, clinical, and pathological characteristics of adrenal incidentalomas, distinguishing benign nonfunctioning lesions from hormonally active tumors and potentially malignant adrenal neoplasms.

- **Explain and interpret** the physiological mechanisms and biochemical abnormalities associated with mild autonomous cortisol secretion, primary aldosteronism, and pheochromocytoma, emphasizing their implications for diagnostic evaluation and perioperative management.

- **Analyze and differentiate** the radiological characteristics of adrenal masses using unenhanced CT, contrast-enhanced imaging, and MRI, identifying features associated with benignity, indeterminate lesions, and increased malignancy risk.

- **Evaluate and compare** current indications, clinical effectiveness, technical limitations, and perioperative outcomes of laparoscopic, retroperitoneoscopic, and robotic-assisted adrenalectomy based on available international evidence.

- **Synthesize and formulate** an integrated clinical decision-making framework combining hormonal findings, radiological characteristics, patient comorbidities, and oncological considerations to support individualized management strategies.

Psychomotor Domain

Given the narrative review design, psychomotor objectives are oriented toward the development of applied clinical reasoning and procedural planning rather than the direct assessment of operative performance.

- **Demonstrate the sequential application** of standardized diagnostic algorithms for adrenal incidentalomas through the interpretation of biochemical results, radiological findings, and representative clinical scenarios.

- **Organize and construct** structured preoperative assessment pathways that integrate endocrine screening, imaging interpretation, surgical risk evaluation, and multidisciplinary consultation.

- **Illustrate and distinguish** the principal anatomical considerations, patient positioning requirements, and procedural stages associated with transperitoneal laparoscopic, posterior retroperitoneoscopic, and robotic-assisted adrenalectomy.

- **Apply established surgical selection criteria** to hypothetical clinical scenarios, identifying appropriate minimally invasive approaches and recognizing situations requiring open surgical evaluation.

Affective Domain

- **Recognize and value** the importance of patient safety, diagnostic accuracy, and individualized clinical assessment when determining whether an incidental adrenal mass requires intervention or surveillance.

- **Promote** multidisciplinary collaboration among endocrinologists, general surgeons, urologists, radiologists, anesthesiologists, and other healthcare professionals involved in adrenal tumor management.

- **Demonstrate commitment** to evidence-based decision-making, ethical clinical practice, and the avoidance of unnecessary diagnostic procedures or surgical interventions.

- **Appraise** the influence of healthcare inequalities, resource availability, and institutional surgical expertise on the implementation of international recommendations, particularly within Latin American healthcare systems.

- **Integrate** patient preferences, quality-of-life considerations, and shared decision-making principles into the evaluation of therapeutic alternatives.

OBJETO DE ESTUDIO

The object of study of this narrative review is the comprehensive diagnostic and therapeutic management of adrenal incidentalomas, with particular emphasis on hormonal evaluation, preoperative radiological characterization, and the selection of minimally invasive surgical approaches. The investigation focuses on the relationship between endocrine functionality, morphological characteristics, oncological risk, and clinical factors that influence the decision to perform adrenalectomy or pursue conservative management.

The target population comprises adult patients with incidentally detected adrenal masses identified through imaging examinations performed for indications unrelated to suspected adrenal pathology. This population includes individuals with nonfunctioning adrenal adenomas, mild autonomous cortisol secretion, primary aldosteronism, pheochromocytomas, and adrenal lesions with indeterminate or suspicious radiological characteristics. Particular consideration is given to patients requiring multidisciplinary evaluation to determine the appropriateness of surgical intervention (Fassnacht et al., 2023; Rowe et al., 2023).

The principal variables examined include biochemical markers of adrenal hormone secretion, tumor size, unenhanced CT attenuation, imaging homogeneity, MRI characteristics, clinical comorbidities, and factors associated with malignancy risk. Surgical variables include indications for adrenalectomy, selection of transperitoneal or retroperitoneal approaches, use of robotic-assisted techniques, and reported perioperative outcomes such as complications, operative duration, and postoperative recovery (Yip et al., 2022; Gan et al., 2022).

The investigation also considers the influence of institutional resources, availability of specialized diagnostic procedures, and surgical expertise on clinical decision-making. Evidence from international guidelines and studies conducted in Latin America is incorporated to examine the applicability of contemporary management strategies across different healthcare environments (Vilar et al., 2008; Castillo et al., 2008; Rebelo et al., 2023).

The scope of this review is restricted to the critical analysis of previously published scientific evidence. It does not involve direct patient recruitment, experimental interventions, or the collection of individual clinical records. Instead, it seeks to identify clinically relevant relationships among endocrine, radiological, and surgical factors to establish a coherent framework for the evaluation and individualized management of adrenal incidentalomas.

METODOLOGÍA

Study Design and Methodological Approach

Edición 5, Año 3, Número 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 5, Year 3, Number 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 5, Año 3, Número 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 5, Year 3, Number 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

This study was designed as a narrative review of the scientific literature, using a structured, evidence-based approach grounded in the scientific method. The methodological framework was developed to examine the relationship between hormonal activity, preoperative radiological characteristics, and surgical decision-making in adult patients with adrenal incidentalomas. The scientific method was selected because it facilitates the formulation of clinically relevant research questions, systematic examination of existing evidence, critical interpretation of findings, and development of conclusions supported by established scientific knowledge.

Unlike systematic reviews and meta-analyses, the present investigation prioritizes the clinical integration of heterogeneous evidence, including international practice guidelines, observational studies, randomized clinical trials, and investigations evaluating minimally invasive adrenal surgery. This approach is appropriate for examining complex clinical decisions that cannot be explained by a single diagnostic parameter or therapeutic outcome.

Research Questions and Analytical Framework

The central research question was formulated as follows: How can hormonal evaluation, preoperative imaging characteristics, and patient-specific clinical factors be integrated to optimize the selection of minimally invasive adrenalectomy in adults with incidentally detected adrenal masses?

Complementary questions addressed the diagnostic relevance of autonomous cortisol secretion, primary aldosteronism, and pheochromocytoma; the ability of CT and MRI to distinguish benign from potentially malignant adrenal lesions; and the clinical circumstances favoring laparoscopic, retroperitoneoscopic, robotic-assisted, or open adrenalectomy.

The analytical framework considered three interconnected dimensions: endocrine functionality, radiological risk stratification, and surgical suitability. These dimensions were evaluated in relation to diagnostic accuracy, perioperative safety, potential therapeutic benefit, and the feasibility of implementing international recommendations in different healthcare environments.

Sources of Scientific Information

The bibliographic framework was based on peer-reviewed medical literature indexed in major scientific databases, particularly PubMed/MEDLINE and journals represented in Scopus. The selected evidence included clinical practice guidelines from recognized endocrine and surgical organizations, systematic reviews, meta-analyses, randomized trials, and observational investigations.

Particular attention was given to publications addressing adrenal incidentalomas, mild autonomous cortisol secretion, adrenal imaging, and minimally invasive adrenalectomy. International studies were complemented by research conducted in Latin America, especially Brazil, Chile, and Argentina, to incorporate regional clinical experience and considerations regarding healthcare resources.

The principal reference framework comprised 20 scientific publications, including the European Society of Endocrinology guidelines, the American Association of Endocrine Surgeons recommendations, and relevant clinical investigations addressing endocrine and surgical management (Fassnacht et al., 2023; Yip et al., 2022; Rowe et al., 2023).

Literature Search Strategy

A reproducible literature search strategy was defined using combinations of controlled vocabulary and free-text terms associated with the principal study domains. The proposed search expressions included *adrenal incidentaloma*, *adrenal mass*, *mild autonomous cortisol secretion*, *hormonal evaluation*, *adrenal imaging*, *adrenalectomy*, *laparoscopic adrenalectomy*, *retroperitoneoscopic adrenalectomy*, and *robotic adrenalectomy*.

Boolean operators AND and OR were incorporated to combine diagnostic and therapeutic concepts. A representative PubMed search strategy was:

("Adrenal Incidentaloma" OR "Adrenal Mass") AND ("Hormonal Evaluation" OR "Cortisol Secretion" OR "Computed Tomography" OR "Magnetic Resonance Imaging" OR "Adrenalectomy" OR "Minimally Invasive Surgery").

The review prioritized publications from 2016 through October 2026, while allowing the inclusion of earlier landmark studies and foundational clinical guidelines when necessary. No geographical restrictions were established. English- and Spanish-language publications were eligible, and relevant Portuguese-language studies were considered when sufficient methodological information was available.

This strategy provides a reproducible framework for literature identification; however, database-specific execution dates, complete search histories, and retrieval counts must be documented before describing the search as exhaustively performed.

Eligibility Criteria

Publications were considered eligible when they addressed at least one of the following domains: hormonal evaluation of adrenal incidentalomas, imaging-based differentiation of adrenal lesions, indications for adrenalectomy, selection of minimally invasive surgical approaches, or perioperative outcomes.

Eligible study designs included clinical guidelines, randomized controlled trials, cohort studies, relevant retrospective investigations, systematic reviews, and meta-analyses. Studies involving adult patients were prioritized.

Publications focused exclusively on pediatric adrenal disease, unrelated retroperitoneal tumors, or adrenal disorders without relevance to incidental mass evaluation were excluded from the principal analytical framework. Case reports and small case series were considered only when they provided relevant information about uncommon clinical presentations or technical considerations not adequately addressed by higher-level evidence.

Evidence Extraction and Critical Appraisal

A standardized extraction framework was defined to organize the information from each publication. The principal categories included author and publication year, study design, population characteristics, endocrine assessment, imaging findings, surgical indications, operative approach, clinical outcomes, and reported limitations.

The methodological quality of the evidence was considered according to study design, population selection, outcome definitions, risk of bias, and consistency with other investigations. Randomized trials and systematic reviews were examined for their ability to support comparative conclusions, while observational investigations were interpreted with attention to potential confounding and selection bias.

Clinical guidelines were evaluated according to their scope, relevance, and consistency with the underlying evidence. Differences among recommendations were retained as areas of uncertainty rather than being interpreted as definitive evidence of superiority.

Data Synthesis and Interpretation

The collected evidence was organized through qualitative thematic synthesis. Findings were classified into hormonal evaluation, radiological characterization, surgical indications, minimally invasive techniques, and individualized therapeutic decision-making.

Because the included literature comprised heterogeneous populations, diagnostic methods, and outcome measures, no new pooled effect estimates or quantitative meta-analysis were planned. Instead, the review focused on identifying areas of agreement, conflicting findings, and unresolved clinical questions.

The interpretation emphasized the distinction between established recommendations and emerging evidence, particularly regarding adrenalectomy for mild autonomous cortisol secretion and the comparative effectiveness of laparoscopic and robotic-assisted procedures.

Reproducibility and Methodological Considerations

Methodological reproducibility was addressed through the definition of research questions, searchable terminology, eligibility criteria, evidence-extraction domains, and a structured analytical framework. Future researchers may apply these procedures to update the review or expand it into a systematic investigation.

Edición 5, Año 3, Número 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 5, Year 3, Number 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

The narrative design permits integration of diverse clinical evidence but does not establish that all eligible studies have been identified. Consequently, the conclusions must be interpreted as an evidence-informed clinical synthesis rather than an exhaustive systematic review.

FASES DEL DESARROLLO

Identification and Delimitation of the Research Problem

The initial phase focused on defining the clinical challenges associated with the increasing detection of adrenal incidentalomas. Particular attention was directed toward the difficulty of distinguishing benign, nonfunctioning adrenal lesions from hormonally active or potentially malignant tumors, as well as determining which patients may benefit from surgical intervention.

The research problem was delimited to three principal dimensions: hormonal evaluation, preoperative radiological characterization, and selection of minimally invasive adrenalectomy. This delimitation was supported by contemporary recommendations emphasizing that adrenal mass management should incorporate endocrine functionality, imaging phenotype, clinical comorbidities, and oncological risk rather than relying exclusively on tumor dimensions (Fassnacht et al., 2023; Yip et al., 2022).

Formulation of Research Questions and Working Hypothesis

The second phase established the principal research question: How can the integration of hormonal findings, radiological characteristics, and patient-specific factors improve the selection of minimally invasive surgical treatment in adults with adrenal incidentalomas?

The guiding working hypothesis proposes that a multidimensional assessment combining biochemical evaluation, imaging-based malignancy stratification, and individualized clinical characteristics provides a more appropriate foundation for therapeutic decisions than isolated anatomical criteria.

This proposition was informed by previous evidence demonstrating the clinical importance of mild autonomous cortisol secretion, the limitations of individual imaging parameters, and the need for individualized surgical indications (Elhassan et al., 2019; Schieda & Siegelman, 2017; Koh et al., 2024).

As a narrative review, the investigation does not seek to statistically test this hypothesis through original patient-level data. Instead, the hypothesis serves as an analytical proposition against which the consistency and limitations of existing evidence can be examined.

Identification and Selection of Scientific Evidence

The third phase established a structured bibliographic framework for identifying relevant publications. Search concepts were organized around adrenal incidentalomas, hormonal assessment, adrenal imaging, malignancy risk, surgical indications, and minimally invasive adrenalectomy.

The evidence framework included international clinical guidelines, randomized trials, observational investigations, systematic reviews, and meta-analyses. Foundational recommendations from endocrine and surgical organizations were prioritized to establish the principal diagnostic and therapeutic standards (Fassnacht et al., 2023; Yip et al., 2022; Rowe et al., 2023).

Studies conducted in Latin America were incorporated into the reference framework to broaden geographical representation and examine the relevance of international recommendations in different clinical environments. Brazilian investigations addressing metabolic abnormalities and adrenal tumor evaluation, together with Chilean experience in laparoscopic adrenalectomy, provided regional perspectives (Vilar et al., 2008; Castillo et al., 2008; Rebelo et al., 2023).

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IECCMEXICO Review

Selection was guided by clinical relevance, methodological characteristics, and direct applicability to the research objectives. The final documentation of database retrieval and screening procedures remains necessary to establish the complete bibliographic selection record.

Critical Appraisal and Thematic Classification

The fourth phase involved organizing the scientific evidence according to the principal clinical dimensions of the review. Hormonal investigations were classified by their relevance to autonomous cortisol secretion, primary aldosteronism, and pheochromocytoma. Imaging studies were examined in relation to lesion attenuation, morphological characteristics, diagnostic uncertainty, and malignancy risk.

Surgical investigations were categorized according to indications for adrenalectomy, operative approach, technical considerations, and perioperative outcomes. Comparative studies of laparoscopic and robotic-assisted procedures were considered alongside international recommendations to distinguish established practices from areas of continuing debate (Gan et al., 2022; Gan et al., 2025).

The appraisal framework also considered study limitations, including retrospective designs, heterogeneous patient populations, differences in diagnostic definitions, and variation in institutional surgical expertise. These factors were treated as important determinants of evidence applicability rather than as interchangeable methodological characteristics.

Integration and Interpretation of Findings

The fifth phase was structured around the synthesis of evidence into a clinically coherent decision-making framework. The first analytical component addressed the identification of hormonally active adrenal lesions and their implications for treatment. The second evaluated imaging characteristics associated with benignity, diagnostic uncertainty, and suspected malignancy. The third examined how these findings influence the selection of surgical or conservative management.

Special consideration was given to mild autonomous cortisol secretion, for which emerging randomized evidence has evaluated the potential benefits of adrenalectomy on cardiometabolic outcomes. The interpretation of these findings requires balancing possible therapeutic improvements against operative risk, patient preferences, and the limitations of available clinical trials (Koh et al., 2024; Ueland et al., 2025).

The synthesis also considered differences in healthcare infrastructure and access to specialized services, particularly within Latin America, where the availability of advanced imaging, endocrine testing, and minimally invasive surgical expertise may vary across institutions.

Development of Clinical Implications and Final Synthesis

The final phase focused on translating the reviewed evidence into clinically applicable considerations for adrenal incidentaloma management. The intended synthesis emphasizes the sequential integration of hormonal evaluation, radiological risk assessment, multidisciplinary discussion, and individualized surgical selection.

Within this framework, conservative surveillance is considered for lesions with sufficiently established benign characteristics and no clinically relevant hormonal activity, while surgical evaluation is prioritized for appropriately selected functioning tumors or lesions with concerning oncological features. The selection of minimally invasive adrenalectomy depends on anatomical feasibility, malignancy risk, patient characteristics, and surgical expertise (Fassnacht et al., 2023; Yip et al., 2022).

This final phase also identifies unresolved questions that warrant additional investigation, including the long-term benefits of adrenalectomy for mild autonomous cortisol secretion, optimal management of indeterminate adrenal lesions, and comparative effectiveness of different minimally invasive techniques.

The resulting framework is intended to support clinical education, facilitate multidisciplinary decision-making, and identify opportunities for future research. It should not be interpreted as a prospectively validated diagnostic algorithm or as evidence of outcomes obtained from an original clinical cohort.

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IECCMEXICO Review

RESULTADOS Y DISCUSIÓN

Figure 1.

Hormonal Evaluation of Adrenal Incidentalomas

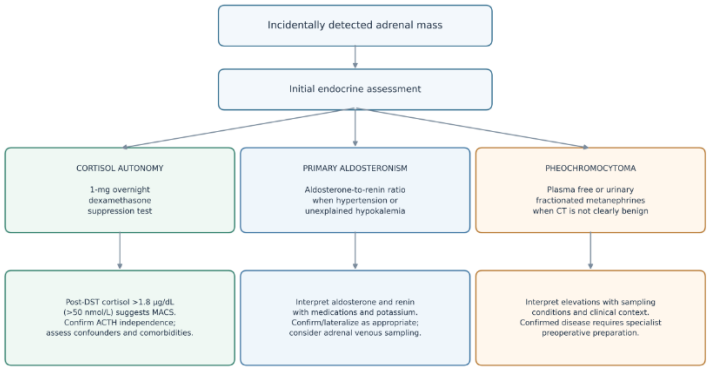


Figure 1 summarizes the three principal endocrine domains that structure the biochemical evaluation of adrenal incidentalomas: autonomous cortisol secretion, primary aldosteronism, and pheochromocytoma. The reviewed evidence consistently shows that hormonal testing is not a secondary step, but a core component of the initial assessment, because clinically inapparent endocrine activity may substantially modify diagnostic classification and subsequent therapeutic planning (Fassnacht et al., 2023; Rowe et al., 2023).

The first branch of the figure addresses **autonomous cortisol secretion**, which is currently regarded as one of the most clinically relevant abnormalities identified in patients with incidentally discovered adrenal masses. Contemporary guidelines recommend the **1-mg overnight dexamethasone suppression test** as the preferred initial screening tool in most adults without overt features of Cushing syndrome. The figure highlights the threshold most commonly used in current practice: a **post-dexamethasone serum cortisol concentration greater than 1.8 µg/dL (50 nmol/L)**, which supports the diagnosis of **mild autonomous cortisol secretion**. This biochemical category is particularly important because many patients do not exhibit classic cushingoid stigmata, yet still demonstrate a greater burden of hypertension, impaired glucose metabolism, obesity, dyslipidemia, and other cardiometabolic disturbances compared with patients harboring clearly nonfunctioning lesions (Fassnacht et al., 2023; Elhassan et al., 2019; Rebelo et al., 2023). Thus, the figure reflects the current understanding that cortisol autonomy should be evaluated not only as a biochemical abnormality, but also in relation to the patient's metabolic and cardiovascular profile.

The figure also indicates that interpretation of cortisol excess should not end with the screening threshold alone. Rather, the biochemical result must be integrated with the clinical context and, when appropriate, with evidence of **ACTH independence**. This is important because the degree of cortisol autonomy may vary across patients, and its clinical expression is frequently subtle. The literature reviewed in this study shows that the diagnostic significance of mild cortisol excess lies less in the presence of overt endocrine syndrome and more in its association with increased comorbidity burden. Randomized and observational studies have further reinforced the relevance of this branch by demonstrating that selected patients with mild autonomous cortisol secretion may experience measurable improvements in blood pressure control, glycemic parameters, or body weight after adrenalectomy, although the magnitude of benefit is variable across studies (Koh et al., 2024; Ueland et al., 2025). For this reason, the figure presents cortisol screening as a foundational domain in the initial work-up of adrenal incidentaloma patients.

The second branch corresponds to **primary aldosteronism**, a condition that should be suspected particularly in patients with **hypertension and/or unexplained hypokalemia**. The figure identifies the **aldosterone-to-renin ratio** as the standard screening test, reflecting its established role in international endocrine practice. However, unlike the cortisol pathway, the interpretation of this test is more dependent on clinical and analytical context, because antihypertensive

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IECCMEXICO Review

medications, plasma potassium concentration, sodium intake, and assay methodology may all influence the result. Therefore, an elevated aldosterone-to-renin ratio should be understood as a screening signal rather than a stand-alone diagnosis, and the figure appropriately indicates the need for **confirmatory testing** and, in selected surgical candidates, **adrenal venous sampling** to establish lateralization (Funder et al., 2016). This step is especially relevant because the mere coexistence of an adrenal nodule and biochemical aldosterone excess does not necessarily prove that the visible lesion is the source of hypersecretion.

From an analytical standpoint, this branch of the figure emphasizes that adrenal incidentaloma evaluation must remain selective and clinically oriented. The literature does not support indiscriminate testing for primary aldosteronism in every patient with an adrenal mass; rather, the diagnostic yield is greatest in individuals with compatible clinical features, particularly hypertension that is resistant, early-onset, or accompanied by hypokalemia. This pattern illustrates a broader principle in adrenal incidentaloma management: endocrine testing should be sufficiently systematic to detect clinically significant disease, while remaining tailored to the patient's presentation and pretest probability (Fassnacht et al., 2023; Rowe et al., 2023).

The third branch addresses the exclusion of **pheochromocytoma**, which remains a critical safety priority in adrenal mass evaluation. Figure 1 presents **plasma free metanephrines** or **urinary fractionated metanephrines** as the principal biochemical studies used when imaging findings are **not clearly benign**. This reflects the evolving consensus that catecholamine-producing tumors must be actively excluded whenever radiological features do not confidently support a lipid-rich adenoma, since failure to diagnose pheochromocytoma before surgery can result in severe intraoperative hemodynamic instability and major perioperative morbidity (Lenders et al., 2014; Fassnacht et al., 2023). In this sense, the figure captures a clinically decisive distinction: endocrine assessment is not performed solely to classify disease, but also to prevent avoidable surgical risk.

The interpretation box beneath this branch emphasizes that **elevated metanephrines support catecholamine excess** and that **preoperative alpha-adrenergic blockade** is required once pheochromocytoma is confirmed. This is consistent with longstanding endocrine and anesthetic principles, as proper preoperative preparation is essential to reduce cardiovascular complications during adrenalectomy. The literature reviewed in this article shows that pheochromocytoma continues to occupy a unique place among incidental adrenal lesions because, unlike many nonfunctioning adenomas, it has immediate implications for both operative planning and perioperative management (Lenders et al., 2014).

Taken together, the three branches shown in Figure 1 illustrate that hormonal evaluation of adrenal incidentalomas is **structured, sequential, and diagnosis-specific**. The evidence does not support a simplistic binary separation between "functioning" and "nonfunctioning" adrenal masses. Instead, current practice recognizes a continuum in which subtle cortisol excess, clinically selective aldosterone screening, and safety-driven exclusion of catecholamine-producing tumors each play distinct roles in patient evaluation. This integrated biochemical framework is consistently supported by recent European, North American, and international recommendations, and it remains central to determining which lesions can be managed conservatively and which require further endocrine investigation or surgical consideration (Fassnacht et al., 2023; Yip et al., 2022; Rowe et al., 2023).

Figure 2.

Radiological Characterization and Malignancy Risk Stratification of Adrenal Incidentalomas

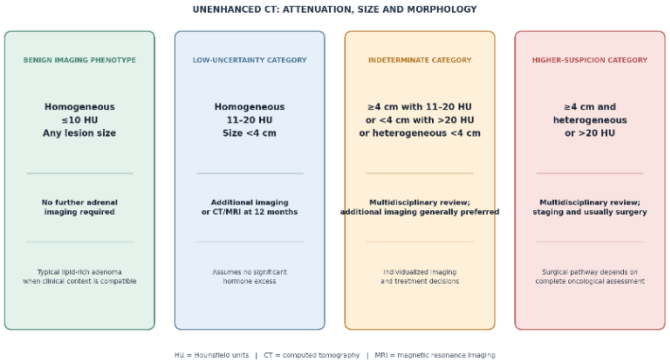


Figure 2 illustrates the principal radiological criteria used to classify incidentally detected adrenal masses according to unenhanced computed tomography attenuation, lesion size, and morphological characteristics. The classification distinguishes four imaging phenotypes that correspond to different degrees of diagnostic certainty and recommended management strategies. These categories are derived primarily from the 2023 European Society of Endocrinology guidelines, which emphasize the integration of imaging characteristics rather than reliance on tumor diameter alone (Fassnacht et al., 2023).

The first category comprises homogeneous adrenal lesions with an attenuation value of 10 Hounsfield units (HU) or less on unenhanced CT. This imaging phenotype is strongly associated with lipid-rich adrenal adenomas and is considered sufficiently characteristic of benignity to avoid additional adrenal imaging, irrespective of lesion size, when the findings are unequivocal. The diagnostic significance of this category arises from the relationship between intracellular lipid content and reduced X-ray attenuation, a characteristic extensively described in radiological investigations of adrenal lesions (Schieda & Siegelman, 2017; Johnson et al., 2009).

The second category includes homogeneous lesions measuring less than 4 cm with unenhanced attenuation values between 11 and 20 HU. These findings introduce a degree of diagnostic uncertainty because lipid-poor adenomas may demonstrate attenuation values above the conventional benign threshold. In the absence of significant hormonal excess, current recommendations favor immediate additional imaging to establish benignity and potentially avoid prolonged surveillance. Alternatively, interval imaging may be considered. The distinction between this category and the first illustrates the importance of attenuation measurements in defining the need for additional radiological characterization (Fassnacht et al., 2023; Nandra et al., 2020).

The third category comprises lesions that do not fulfill the criteria for either unequivocal benignity or the higher-suspicion group. Examples include adrenal masses smaller than 4 cm with attenuation above 20 HU or heterogeneous lesions without other high-risk features. These findings may occur in lipid-poor adenomas, pheochromocytomas, and other adrenal neoplasms, creating potential overlap between benign and malignant entities. Consequently, multidisciplinary evaluation and additional imaging are generally considered appropriate to clarify the diagnostic classification. MRI chemical-shift sequences may contribute to identifying intracellular lipid, although their diagnostic performance depends on lesion composition and technical characteristics (Schieda & Siegelman, 2017; Nandra et al., 2020).

The fourth category identifies adrenal lesions measuring at least 4 cm that additionally demonstrate heterogeneous morphology or unenhanced attenuation exceeding 20 HU. These characteristics are associated with greater concern for malignancy and commonly prompt multidisciplinary evaluation, further staging, and consideration of surgical treatment. Nevertheless, radiological suspicion does not establish a definitive histopathological diagnosis. Management also depends on endocrine findings, previous malignancy, evidence of local invasion, and assessment of whether complete surgical resection is technically feasible (Fassnacht et al., 2023; Yip et al., 2022).

An important finding represented by the figure is that **tumor size and imaging attenuation should be interpreted together**. A small lesion with suspicious morphological characteristics may require further investigation, whereas a larger homogeneous lesion with unequivocally benign attenuation may not require additional adrenal imaging.

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IECCMEXICO Review

Similarly, imaging findings alone cannot determine hormonal functionality, reinforcing the need to interpret radiological characteristics alongside biochemical evaluation (Rowe et al., 2023; Fassnacht et al., 2023).

Figure 3.

Cardiometabolic Outcomes Following Adrenalectomy in Patients With Mild Autonomous Cortisol Secretion

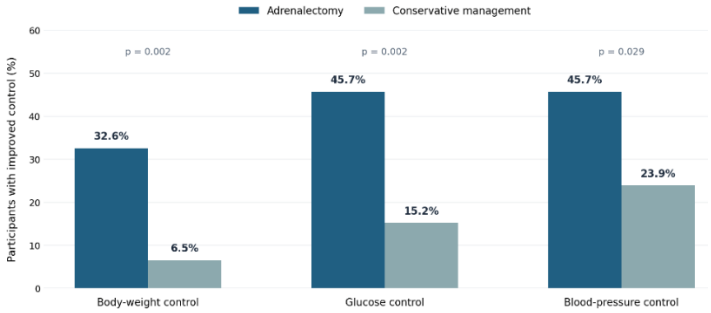


Figure 3 presents a comparative analysis of cardiometabolic improvements following adrenalectomy versus conservative management in patients with mild autonomous cortisol secretion (MACS). The graphical representation is based on the randomized COAR study reported by Koh et al. (2024), which investigated changes in body-weight control, glucose regulation, and blood-pressure management. The trial originally randomized 132 patients, while the comparative percentages displayed in the figure correspond to the age- and sex-matched analysis involving 46 patients in each treatment group. Therefore, the results represent published trial findings rather than pooled estimates derived from multiple investigations (Koh et al., 2024).

The first outcome evaluated was **improvement in body-weight control**, which occurred in 32.6% of patients undergoing adrenalectomy compared with 6.5% of conservatively managed patients (p = 0.002). This corresponds to an absolute difference of 26.1 percentage points between groups. The finding demonstrates a statistically significant difference in the frequency of improved weight control among the analyzed participants. In the study's multivariable analysis, adrenalectomy was independently associated with improved weight control, with an odds ratio of 10.38 (95% CI: 2.09–51.52; p = 0.004). Body mass index and post-dexamethasone cortisol concentrations were also identified as associated variables, indicating that the observed outcomes were evaluated in relation to both baseline metabolic characteristics and biochemical indicators of cortisol autonomy (Koh et al., 2024).

The second outcome concerns **glucose control**, for which improvement was documented in 45.7% of surgically treated patients compared with 15.2% of patients receiving conservative management (p = 0.002). The absolute difference of 30.5 percentage points represented the largest between-group separation among the three endpoints shown in the figure. Adrenalectomy was independently associated with improved glucose control in the COAR analysis (OR = 5.30; 95% CI: 1.63–17.25; p = 0.006), while diabetes mellitus was also associated with this outcome. These findings provide quantitative evidence of differences in glucose-related outcomes between the two treatment strategies within the analyzed cohort (Koh et al., 2024).

The third parameter, **blood-pressure control**, improved in 45.7% of patients in the adrenalectomy group and 23.9% of patients in the conservative group (p = 0.029). This represents an absolute difference of 21.8 percentage points. Although the between-group comparison was statistically significant, the multivariable analysis did not establish adrenalectomy as an independently significant predictor of improved blood-pressure control at the conventional threshold (OR = 2.27; 95% CI: 0.87–5.94; p = 0.095). Pre-existing hypertension demonstrated a stronger independent association with the outcome, emphasizing the importance of distinguishing unadjusted comparisons from adjusted statistical findings (Koh et al., 2024).

Additional evidence from the randomized trial conducted by Ueland et al. (2025) offers an important complementary perspective. In that investigation, 43 patients with MACS were randomized to adrenalectomy (n = 21) or conservative management (n = 22). After two years, biochemical normalization following the dexamethasone suppression test was

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IECCMEXICO Review

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IECCMEXICO Review

observed in 19 of 21 surgically treated patients compared with 2 of 22 patients in the conservative group ($p < 0.01$). Furthermore, improvement in office blood pressure and antihypertensive medication requirements was observed in 9 of 12 adrenalectomy patients and 4 of 15 conservatively managed patients ($p = 0.01$). However, when 24-hour ambulatory blood-pressure measurements and medication requirements were considered, the corresponding improvement rates were 5 of 11 and 6 of 15 patients, respectively ($p = 0.78$), indicating that the observed difference depended partly on the assessment method (Ueland et al., 2025).

Regarding glucose metabolism, Ueland et al. (2025) reported that patients without established type 2 diabetes demonstrated lower 120-minute glucose concentrations during oral glucose tolerance testing in the adrenalectomy group compared with conservatively managed participants (6.2 versus 7.3 mmol/L; $p = 0.04$). Nevertheless, changes from baseline did not consistently demonstrate significant between-group differences, and no statistically significant improvement in overall quality-of-life measurements was established. These findings illustrate the variation in reported cardiometabolic outcomes across randomized investigations, particularly when different outcome definitions and measurement methods are used.

More recent evidence from the randomized CHIRACIC trial, published by Tabarin et al. (2026), further demonstrates this variability. Among 48 randomized patients, clinically meaningful weight reduction exceeding 5% was reported in 21% of overweight or obese surgical patients compared with 4% of conservatively managed patients. Improvement in glycemic status occurred in 44% and 33% of dysglycemic participants, respectively. However, the investigators did not identify statistically significant between-group improvements in the principal anthropometric and metabolic parameters, and quality-of-life changes were not significantly different. These findings should be interpreted separately from those of the COAR trial because of differences in sample size, follow-up duration, and outcome definitions (Tabarin et al., 2026).

Figure 4.

Comparative Perioperative Outcomes of Laparoscopic and Robotic-Assisted Adrenalectomy

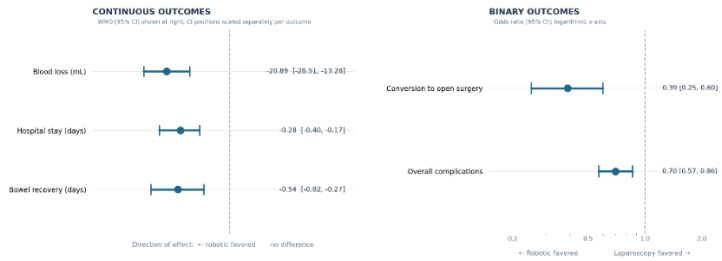


Figure 4 presents the comparative perioperative outcomes of robotic-assisted adrenalectomy (RA) and conventional laparoscopic adrenalectomy (LA), based on the systematic review and meta-analysis conducted by Gan et al. (2025). The study included 45 investigations comprising 7,225 patients and evaluated several clinically relevant endpoints, including estimated blood loss, hospital length of stay, postoperative bowel recovery, conversion to open surgery, and overall complication rates. The figure displays pooled effect estimates and their corresponding 95% confidence intervals, allowing the direction and statistical precision of the reported associations to be examined. Negative weighted mean differences and odds ratios below 1.0 indicate results favoring robotic-assisted adrenalectomy for the outcomes represented.

The first parameter concerns **estimated intraoperative blood loss**, for which robotic-assisted adrenalectomy demonstrated a weighted mean difference of −20.89 mL (95% CI: −28.51 to −13.28; $p < 0.01$) compared with conventional laparoscopic surgery. The confidence interval remained entirely below the null value, indicating a statistically significant difference between approaches. Although the absolute magnitude of this reduction was relatively modest, the finding was consistent with the direction reported in earlier investigations. The 2022 meta-analysis by Gan et al., which included 26 studies and 2,985 patients, similarly documented lower estimated blood loss with robotic surgery (WMD = −18.25 mL; 95% CI: −27.85 to −8.65). These findings establish a consistent pattern

across the two quantitative syntheses, although the included study populations and selection criteria were not identical (Gan et al., 2022; Gan et al., 2025).

Hospital length of stay constituted the second continuous outcome. The 2025 meta-analysis reported a weighted mean difference of −0.28 days (95% CI: −0.40 to −0.17; $p < 0.01$), corresponding to a statistically significant shorter hospital stay in patients undergoing robotic-assisted adrenalectomy. An earlier pooled analysis reported a difference of −0.45 days (95% CI: −0.57 to −0.33), similarly favoring robotic surgery (Gan et al., 2022).

Figure 5.

Integrated Clinical Decision-Making Pathway for Adrenal Incidentalomas

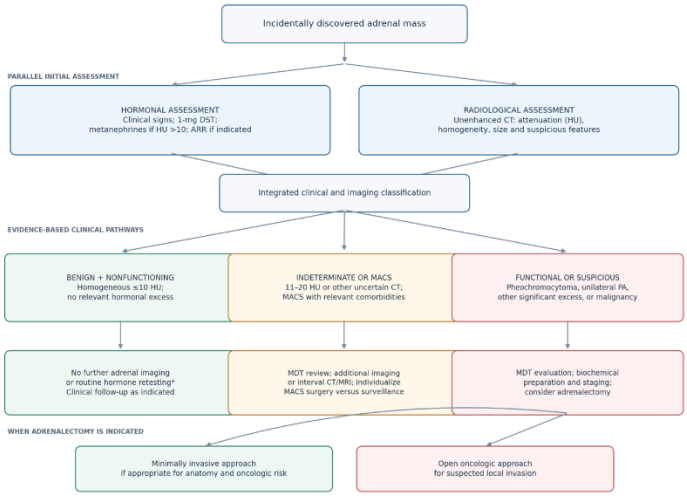


Figure 5 integrates the principal diagnostic and therapeutic findings identified throughout the literature into a structured clinical decision-making pathway for adults presenting with adrenal incidentalomas. The proposed framework combines hormonal assessment, radiological characterization, multidisciplinary evaluation, and surgical selection. Its organization reflects the contemporary understanding that adrenal incidentalomas cannot be adequately classified using tumor size, radiological appearance, or endocrine activity independently. Instead, these parameters must be interpreted together to establish the most appropriate management strategy for each clinical presentation (Fassnacht et al., 2023; Yip et al., 2022; Rowe et al., 2023).

The initial component of the figure demonstrates the parallel application of **hormonal and radiological assessment** following the incidental identification of an adrenal mass. From an endocrinological perspective, evaluation begins with a clinical examination directed toward manifestations of cortisol excess, catecholamine hypersecretion, and mineralocorticoid abnormalities. The 1-mg overnight dexamethasone suppression test represents the principal screening procedure for autonomous cortisol secretion in most patients, while aldosterone-to-renin ratio testing is indicated when hypertension or unexplained hypokalemia is present. Biochemical exclusion of pheochromocytoma is particularly important when unenhanced CT findings are not characteristic of a benign lipid-rich adenoma (Fassnacht et al., 2023; Funder et al., 2016; Lenders et al., 2014).

In parallel, radiological assessment establishes the structural characteristics of the adrenal lesion. Unenhanced CT attenuation, measured in Hounsfield units, is a central component of this classification. Homogeneous adrenal masses with attenuation values of 10 HU or less are strongly associated with benign lipid-rich adenomas, whereas lesions demonstrating higher attenuation, heterogeneous morphology, or suspicious anatomical characteristics require additional consideration. The reviewed radiological literature supports the importance of combining attenuation measurements with lesion morphology and relevant clinical findings rather than interpreting tumor diameter as an isolated indicator of malignancy (Schieda & Siegelman, 2017; Nandra et al., 2020; Johnson et al., 2009).

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IECCMEXICO Review

Following integration of these findings, the algorithm distinguishes three principal management pathways. The first corresponds to **benign, nonfunctioning adrenal lesions**, particularly homogeneous masses with unequivocally benign CT characteristics and no clinically relevant hormonal excess. In this category, routine additional adrenal imaging is generally unnecessary. Current recommendations also discourage repeated hormonal testing in patients whose initial biochemical evaluation is normal unless new clinical manifestations develop or relevant comorbidities worsen. This pathway represents the group in which conservative management can be established with a high degree of diagnostic confidence (Fassnacht et al., 2023; Rowe et al., 2023).

The second pathway includes **indeterminate adrenal masses and lesions associated with mild autonomous cortisol secretion**. This group requires more individualized assessment because imaging uncertainty and subtle endocrine abnormalities do not necessarily establish an immediate indication for surgery. For radiologically indeterminate lesions, additional CT or MRI characterization may improve diagnostic classification, while interval imaging remains an option when the lesion cannot be conclusively categorized. In patients with MACS, assessment also incorporates hypertension, diabetes mellitus, obesity, cardiovascular disease, and the severity of potentially cortisol-associated comorbidities. Evidence from clinical investigations has demonstrated differences in metabolic outcomes between patients undergoing adrenalectomy and those receiving conservative management, although the magnitude of these differences varies according to the population and outcome evaluated (Elhassan et al., 2019; Koh et al., 2024; Ueland et al., 2025).

The figure places particular emphasis on **multidisciplinary evaluation**, which represents a critical component of decision-making for indeterminate lesions, clinically relevant hormonal excess, and suspected malignancy. Collaboration among endocrinologists, radiologists, surgeons, and other specialists allows biochemical abnormalities to be interpreted alongside anatomical findings and operative risk. This is especially important when imaging characteristics are equivocal or when the potential benefits of adrenalectomy must be balanced against comorbidities, advanced age, or limited physiological reserve. The European Society of Endocrinology specifically recommends multidisciplinary discussion when imaging is inconsistent with a benign lesion, clinically meaningful hormone excess is present, surgery is being considered, or significant tumor growth occurs during surveillance (Fassnacht et al., 2023).

The third pathway identifies **functionally active adrenal tumors and lesions with concerning oncological features**. Confirmed pheochromocytomas, appropriately lateralized unilateral primary aldosteronism, and selected cortisol-producing tumors represent conditions in which adrenalectomy may provide definitive treatment. However, the necessary preoperative evaluation differs according to the underlying endocrine disorder. Pheochromocytoma requires specific cardiovascular preparation, including alpha-adrenergic blockade, whereas primary aldosteronism requires careful confirmation of unilateral hormone production before definitive surgical treatment. Similarly, patients with suspected adrenocortical carcinoma require appropriate oncological staging and assessment of local tumor extension before selecting an operative technique (Lenders et al., 2014; Funder et al., 2016; Yip et al., 2022).

An additional distinction represented in Figure 5 concerns the selection between **minimally invasive and open adrenalectomy**. Minimally invasive approaches, including laparoscopic and robotic-assisted adrenalectomy, are established options for appropriately selected adrenal tumors when complete and safe resection is feasible. Nevertheless, their suitability depends on tumor characteristics, anatomical relationships, previous surgical history, and operator expertise. In contrast, tumors demonstrating suspected invasion of adjacent structures generally require an oncologically appropriate open approach to maximize the likelihood of complete resection while minimizing the risk of capsular disruption or tumor spillage (Yip et al., 2022; Castillo et al., 2008; Gan et al., 2022).

The algorithm also reflects the importance of differentiating radiological suspicion from histopathologically confirmed malignancy. Although heterogeneous morphology, elevated attenuation, and larger tumor dimensions may increase concern for malignancy, these features do not independently establish a definitive diagnosis. Consequently, the pathway incorporates multidisciplinary assessment and further staging before operative selection. This distinction preserves the diagnostic relationship between imaging characteristics, endocrine findings, and surgical management without assuming that every radiologically suspicious lesion represents adrenal carcinoma (Fassnacht et al., 2023; Nandra et al., 2020).

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IECCMEXICO Review

Finally, the integrated structure is consistent with the international and Latin American evidence examined in this review. Investigations conducted in Brazil, Chile, and Argentina have contributed information on adrenal tumor characteristics, metabolic abnormalities, and surgical experience, complementing the broader international recommendations. These studies demonstrate the relevance of a comprehensive clinical approach while highlighting the diversity of patient populations and institutional practices represented in the available literature (Vilar et al., 2008; Castillo et al., 2008; Rebelo et al., 2023; Chervin et al., 2007).

DISCUSIÓN

The findings of this narrative review demonstrate that the management of adrenal incidentalomas has evolved from a predominantly anatomical approach toward an integrated clinical model incorporating endocrine functionality, radiological characterization, oncological risk, and individualized surgical selection. The evidence synthesized across the five figures supports the importance of distinguishing benign, nonfunctioning adrenal lesions from tumors associated with clinically relevant hormonal activity or malignant potential. Nevertheless, substantial uncertainty persists regarding the management of mild autonomous cortisol secretion (MACS), radiologically indeterminate masses, and the comparative advantages of minimally invasive surgical techniques. These uncertainties are particularly relevant because diagnostic and therapeutic decisions may have long-term consequences for cardiometabolic health, perioperative safety, and healthcare resource utilization (Fassnacht et al., 2023; Yip et al., 2022; Rowe et al., 2023).

Integration of Hormonal Evaluation and Clinical Risk

One of the principal findings of this review is that biochemical evaluation remains indispensable even when adrenal lesions are identified in patients without overt endocrine manifestations. The diagnostic framework presented in Figure 1 demonstrates that autonomous cortisol secretion, primary aldosteronism, and pheochromocytoma require distinct screening strategies and different interpretations of biochemical abnormalities. This finding is consistent with contemporary international guidelines, which emphasize that adrenal morphology cannot reliably predict hormonal functionality and that endocrine evaluation should be adapted to the patient's clinical presentation (Fassnacht et al., 2023; Funder et al., 2016; Lenders et al., 2014).

The recognition of MACS represents one of the most significant conceptual developments in adrenal incidentaloma management. Historically, adrenal lesions without overt Cushing syndrome were frequently categorized as clinically nonfunctioning. However, evidence from observational investigations and systematic reviews has demonstrated that relatively subtle cortisol autonomy may be associated with hypertension, impaired glucose metabolism, and increased cardiometabolic morbidity. Elhassan et al. (2019) identified clinically relevant differences in the natural history of adrenal incidentalomas according to cortisol secretion status, supporting the need to distinguish mild biochemical autonomy from unequivocally nonfunctioning lesions.

These findings are reinforced by investigations conducted in Latin America. Ribeiro Cavalari et al. (2018) examined the relationship between adrenal incidentalomas and metabolic syndrome, while Rebelo et al. (2023) evaluated clinical and metabolic differences between apparently nonfunctioning adrenal lesions and those associated with autonomous cortisol secretion. Together, these studies support the importance of examining metabolic abnormalities in patients whose adrenal lesions would otherwise appear clinically silent.

Nevertheless, the association between cortisol autonomy and cardiometabolic disease does not necessarily demonstrate that cortisol excess is the sole cause of the observed abnormalities. Age, obesity, baseline cardiovascular risk, and coexisting metabolic disorders may contribute to these relationships. Consequently, the interpretation of hormonal findings requires consideration of potential confounding factors, particularly when evaluating observational studies. This distinction is essential to avoid attributing all metabolic abnormalities to an adrenal lesion without sufficient clinical evidence.

Radiological Characterization and the Limitations of Tumor Size

The radiological findings summarized in Figure 2 support the increasing importance of unenhanced CT attenuation and lesion homogeneity in the characterization of adrenal incidentalomas. The conventional threshold of 10 HU or less

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IECCMEXICO Review

remains a highly reliable characteristic of lipid-rich adrenal adenomas, particularly when the lesion is homogeneous and the clinical context is compatible with benign disease. Current European recommendations recognize that such lesions generally do not require additional imaging, regardless of tumor dimensions (Fassnacht et al., 2023).

This represents an important departure from earlier management strategies in which tumor diameter frequently served as the principal determinant of additional investigation or surgical intervention. Although lesion size remains clinically relevant, the contemporary evidence indicates that it should not be interpreted independently of attenuation values, morphological characteristics, and oncological context.

Schieda and Siegelman (2017) demonstrated the diagnostic value of CT and MRI in characterizing adrenal nodules, while Nandra et al. (2020) emphasized the technical and interpretive limitations that may influence radiological classification. These investigations are particularly relevant to indeterminate lesions, for which lipid-poor adenomas and potentially malignant tumors may demonstrate overlapping imaging characteristics.

Consequently, a lesion measuring less than 4 cm cannot automatically be considered benign, particularly when heterogeneous morphology or elevated attenuation is present. Conversely, a larger homogeneous lesion with unequivocally benign imaging characteristics does not necessarily require surgical removal. This distinction supports the adoption of multidimensional radiological assessment rather than uniform size-based recommendations.

Another important consideration concerns the potential consequences of excessive imaging surveillance. Repeated examinations may increase healthcare expenditures, patient anxiety, and exposure to ionizing radiation without providing proportional clinical benefit in lesions already characterized as benign. Conversely, insufficient evaluation of suspicious lesions may delay appropriate oncological management. The current evidence therefore favors imaging strategies that reflect the degree of diagnostic uncertainty rather than applying identical follow-up schedules to all patients (Fassnacht et al., 2023; Rowe et al., 2023).

Clinical Significance of Adrenalectomy in Mild Autonomous Cortisol Secretion

The findings presented in Figure 3 provide quantitative evidence supporting the potential cardiometabolic benefits of adrenalectomy in selected patients with MACS. The randomized trial conducted by Koh et al. (2024) demonstrated significantly higher frequencies of improved body-weight control, glucose regulation, and blood-pressure control among surgically treated patients compared with those receiving conservative management.

In the age- and sex-matched comparison, improvement in body-weight control occurred in 32.6% of surgically treated patients compared with 6.5% of controls. Improved glucose control was observed in 45.7% versus 15.2%, while improved blood-pressure control occurred in 45.7% versus 23.9%, respectively. These findings suggest that surgical correction of autonomous cortisol secretion may be associated with clinically measurable improvements in selected metabolic outcomes (Koh et al., 2024).

However, interpretation of these findings requires attention to the distinction between statistical significance and clinical relevance. Improvements in metabolic parameters do not necessarily establish long-term reductions in cardiovascular mortality, major cardiovascular events, or overall mortality. Furthermore, the effects of adrenalectomy may differ according to the duration of cortisol excess, baseline comorbidities, patient age, and the reversibility of established metabolic disease.

The randomized investigation conducted by Ueland et al. (2025) provided additional evidence of improved biochemical cortisol regulation following adrenalectomy, together with differences in selected cardiometabolic outcomes. Nevertheless, some results varied according to the measurement methods employed, particularly in the assessment of blood pressure.

This variability illustrates that the benefits of surgery cannot be assumed to be uniform across all patients with MACS. The decision to perform adrenalectomy should therefore consider the severity and progression of potentially cortisol-related comorbidities, the degree and persistence of autonomous cortisol secretion, patient preferences, and operative risk.

Edición 5, Año 3, Número 2, 2026
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Revista IECCMEXICO
Edition 5, Year 3, Number 2, 2026
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IECCMEXICO Review

The European Society of Endocrinology guidelines support this individualized approach, recommending consideration of surgery in patients with MACS and relevant comorbidities rather than establishing adrenalectomy as a universal treatment (Fassnacht et al., 2023).

An additional research priority is determining which clinical characteristics most accurately identify patients likely to benefit from surgery. Future investigations should evaluate whether combinations of biochemical cortisol measurements, metabolic profiles, and cardiovascular risk factors can improve the prediction of postoperative outcomes.

Comparative Effectiveness of Minimally Invasive Adrenalectomy

The comparative surgical findings summarized in Figure 4 demonstrate that robotic-assisted and conventional laparoscopic adrenalectomy are both established minimally invasive techniques, although differences have been reported in several perioperative outcomes.

The systematic review and meta-analysis by Gan et al. (2025), incorporating 45 studies and 7,225 patients, reported advantages associated with robotic-assisted adrenalectomy in estimated blood loss, hospital length of stay, bowel recovery time, conversion to open surgery, and overall complications.

The reported reductions in estimated blood loss and hospital stay were statistically significant, although their absolute magnitudes were relatively modest. Similarly, the lower pooled odds of conversion and overall complications favored robotic surgery, but these findings should be interpreted within the methodological limitations of comparative surgical studies.

An earlier meta-analysis by Gan et al. (2022) also identified favorable outcomes for robotic-assisted adrenalectomy in selected perioperative measures. The consistency between these investigations suggests that robotic surgery may offer technical advantages in particular operative circumstances, especially where anatomical complexity or difficult dissection is anticipated.

Nevertheless, several factors limit the interpretation of these comparisons. Robotic platforms are frequently concentrated in specialized centers, where surgical teams may possess substantial experience and institutions may have established perioperative protocols. Consequently, differences in outcomes may partly reflect center characteristics, patient selection, surgeon expertise, or institutional resources rather than the surgical platform alone.

Furthermore, statistically significant reductions in blood loss or hospitalization do not necessarily establish the overall superiority or cost-effectiveness of robotic adrenalectomy. Acquisition expenses, maintenance requirements, disposable instruments, operating room availability, and training costs are important considerations that may substantially influence healthcare implementation.

For this reason, conventional laparoscopic adrenalectomy remains a highly relevant technique, particularly in healthcare systems where robotic platforms are not routinely available. Surgical effectiveness should be evaluated through a balance of technical feasibility, patient safety, oncological adequacy, resource availability, and institutional expertise rather than through isolated comparisons of perioperative endpoints.

Surgical Selection and Oncological Safety

The integrated decision-making pathway presented in Figure 5 emphasizes that selecting a minimally invasive surgical approach requires more than confirming an indication for adrenalectomy. Tumor characteristics, anatomical relationships, suspected malignancy, and the potential for complete resection must also be considered.

For benign functioning tumors and appropriately selected adrenal masses without evidence of local invasion, minimally invasive adrenalectomy generally provides favorable postoperative recovery and reduced surgical morbidity compared with traditional open procedures. However, suspected invasive adrenocortical carcinoma presents a different clinical situation in which oncological completeness takes priority over the benefits of minimally invasive access (Yip et al., 2022).

Edición 5, Año 3, Número 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 5, Year 3, Number 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

The risk of tumor rupture, capsular disruption, or incomplete resection must be carefully considered when malignancy is suspected. Consequently, open adrenalectomy remains important when there is evidence of local invasion or when minimally invasive surgery may compromise oncological principles.

The surgical experience reported by Castillo et al. (2008) contributes a Latin American perspective to the relationship between tumor size and laparoscopic adrenalectomy. Their findings are relevant to the broader recognition that technical feasibility cannot be established through tumor dimensions alone.

The selection between transperitoneal laparoscopy, posterior retroperitoneoscopy, and robotic-assisted surgery should therefore be individualized. Previous abdominal operations, body habitus, tumor location, adjacent anatomical structures, and surgeon experience may influence procedural selection and technical complexity.

These considerations reinforce the importance of multidisciplinary evaluation and appropriate referral pathways for complex adrenal tumors.

Relevance to Latin American Healthcare Systems

The inclusion of Latin American investigations represents an important component of the present review because the practical implementation of international recommendations may differ according to healthcare infrastructure, availability of specialized services, and institutional experience.

Studies conducted in Brazil have contributed evidence concerning adrenal incidentaloma characteristics, metabolic abnormalities, and diagnostic evaluation. Vilar et al. (2008), Ribeiro Cavalari et al. (2018), and Rebelo et al. (2023) provide regional observations that complement findings from larger international investigations.

Similarly, the surgical experience reported by Castillo et al. (2008) demonstrates the relevance of Latin American contributions to the evaluation of minimally invasive adrenalectomy, while the Argentine experience described by Chervin et al. (2007) provides additional clinical context regarding the investigation of adrenal incidentalomas.

However, these studies should not be interpreted as representative of all Latin American healthcare systems. Differences in study design, sample size, institutional characteristics, and publication period limit direct regional generalization.

In settings where access to advanced endocrine testing, specialized imaging, adrenal venous sampling, or robotic surgery is restricted, the implementation of clinical pathways may require adaptations based on available resources. Nevertheless, the fundamental principles of biochemical assessment, malignancy stratification, multidisciplinary evaluation, and oncologically appropriate treatment remain applicable.

The development of regional referral networks, specialized adrenal surgery programs, and standardized diagnostic protocols may help reduce disparities in care. Additional multicenter investigations involving Latin American institutions would be valuable for examining diagnostic delays, surgical outcomes, resource utilization, and long-term patient follow-up.

Methodological Limitations and Future Research Directions

Several limitations should be considered when interpreting the findings of this review. First, the narrative design permits integration of heterogeneous evidence but does not provide the exhaustive study identification or formal pooled statistical analysis characteristic of a systematic review and meta-analysis. Consequently, the results should be interpreted as a structured clinical synthesis rather than a comprehensive quantitative estimate of diagnostic or therapeutic effectiveness.

Second, the included publications differ in study design, diagnostic definitions, clinical populations, and outcome measurements. These variations are particularly important in studies addressing MACS, where differences in cortisol thresholds, comorbidity definitions, and follow-up duration may influence the reported prevalence of metabolic abnormalities and the apparent benefits of surgery.

Edición 5, Año 3, Número 2, 2026
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Revista IECCMEXICO
Edition 5, Year 3, Number 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 5, Año 3, Número 2, 2026
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Revista IECCMEXICO

Edition 5, Year 3, Number 2, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Third, much of the comparative evidence concerning laparoscopic and robotic-assisted adrenalectomy originates from observational investigations. Such studies may be affected by selection bias, confounding, institutional differences, and variation in surgical expertise. Although meta-analyses increase the volume of available evidence, pooling observational studies does not eliminate their underlying methodological limitations (Gan et al., 2022; Gan et al., 2025).

Fourth, the long-term outcomes of adrenalectomy in patients with MACS remain incompletely established. While randomized studies have provided evidence of improvements in selected cardiometabolic outcomes, further research is required to determine whether these benefits translate into sustained reductions in cardiovascular events, mortality, or healthcare utilization.

Fifth, the representation of Latin American populations remains comparatively limited in the available evidence. Most regional investigations involve selected clinical populations or individual institutions, restricting the extent to which their findings can be generalized across countries with different healthcare systems and surgical resources.

Future research should prioritize larger prospective multicenter studies, standardized definitions of hormonal functionality, longer follow-up periods, and direct comparisons of surgical strategies. Additional investigations evaluating quality of life, postoperative adrenal insufficiency, cost-effectiveness, and patient-reported outcomes would also strengthen the evidence supporting individualized treatment selection.

Finally, the development and external validation of clinical prediction models integrating hormonal measurements, imaging characteristics, comorbidity burden, and surgical risk may improve decision-making. Such models should be evaluated across geographically and socioeconomically diverse populations before being incorporated into routine clinical pathways.

CONCLUSIÓN

Adrenal incidentalomas represent a complex clinical entity requiring an integrated diagnostic and therapeutic approach that combines hormonal evaluation, radiological characterization, malignancy risk stratification, and individualized surgical planning. The findings of this narrative review demonstrate that optimal management cannot be determined solely by tumor size or anatomical appearance, but instead depends on the interaction between endocrine functionality, imaging characteristics, patient comorbidities, and oncological considerations.

Hormonal assessment remains a fundamental component of the diagnostic process, particularly for identifying mild autonomous cortisol secretion, primary aldosteronism, and pheochromocytoma. The recognition of these conditions is essential because clinically significant hormonal abnormalities may occur without overt endocrine manifestations. Similarly, radiological evaluation using unenhanced computed tomography and complementary imaging techniques provides valuable information for distinguishing benign adrenal adenomas from indeterminate or potentially malignant lesions, allowing more appropriate selection of surveillance or surgical intervention (Fassnacht et al., 2023; Rowe et al., 2023).

The reviewed evidence indicates that adrenalectomy may provide meaningful cardiometabolic benefits in selected patients with mild autonomous cortisol secretion, particularly regarding blood-pressure regulation, glucose metabolism, and weight control. Nevertheless, variability among clinical investigations reinforces the need for individualized treatment decisions, as the long-term impact of surgery on cardiovascular events and mortality remains incompletely established (Elhassan et al., 2019; Koh et al., 2024; Ueland et al., 2025).

Minimally invasive adrenalectomy represents an effective therapeutic option for appropriately selected adrenal tumors. Both laparoscopic and robotic-assisted approaches have demonstrated favorable perioperative outcomes, although the available comparative evidence suggests that differences between techniques should be interpreted in relation to surgical expertise, patient selection, anatomical complexity, and institutional resources. Importantly, suspected locally invasive adrenal malignancy requires an oncologically appropriate surgical strategy in which complete tumor resection takes precedence over the advantages of minimally invasive access (Yip et al., 2022; Gan et al., 2022; Gan et al., 2025).

The integration of international recommendations with clinical investigations from Latin America highlights the importance of developing diagnostic and surgical pathways that remain scientifically rigorous while accounting for differences in healthcare infrastructure and access to specialized services. Multidisciplinary collaboration among endocrinologists, surgeons, urologists, radiologists, and other specialists is essential for ensuring diagnostic accuracy, appropriate surgical indications, and patient-centered care.

In conclusion, **the optimal management of adrenal incidentalomas depends on accurate hormonal and radiological characterization followed by individualized selection of conservative or surgical treatment**. Future research should prioritize prospective multicenter investigations, standardized diagnostic criteria, long-term cardiometabolic outcomes, and comparative assessments of minimally invasive techniques, with greater participation from Latin American institutions. Such efforts may strengthen clinical decision-making, reduce unnecessary interventions, and improve the safety, effectiveness, and accessibility of adrenal tumor management.

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Revista IECCMEXICO
Edition 5, Year 3, Number 2, 2026
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IECCMEXICO Review

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IECCMEXICO Review