Exploration of Endocrine and Metabolic Diseases

Open Exploration

Open Access Review

Cardiovascular effects of endocrine hypertension: insights from primary aldosteronism, pheochromocytoma, and Cushing syndrome

Mehmet Murat Şahin[1], Macit Kalçık[2*], Mucahit Yetim[2], Muhammet Cihat Çelik[1], Lütfü Bekar[2], Yusuf Karavelioğlu[2]

[1]Department of Cardiology, Hitit University Erol Olçok Education and Research Hospital, Corum 19040, Turkey
[2]Department of Cardiology, Faculty of Medicine, Hitit University, Corum 19040, Turkey

***Correspondence:** Macit Kalçık, Department of Cardiology, Faculty of Medicine, Hitit University, Buharaevler Mah., Buhara 25. Sok., No: 1/A, Daire: 22, Corum 19040, Turkey. macitkalcik@yahoo.com
Academic Editor: George P. Chrousos, National and Kapodistrian University of Athens, Greece
Received: October 10, 2025 **Accepted:** November 17, 2025 **Published:** January 8, 2026

Cite this article: Şahin MM, Kalçık M, Yetim M, Çelik MC, Bekar L, Karavelioğlu Y. Cardiovascular effects of endocrine hypertension: insights from primary aldosteronism, pheochromocytoma, and Cushing syndrome. Explor Endocr Metab Dis. 2026;3:101454. https://doi.org/10.37349/eemd.2026.101454

Abstract

Endocrine hypertension (HT) includes a group of secondary hypertensive disorders caused by hormonal excess, primarily primary aldosteronism (PA), pheochromocytoma and paraganglioma (PPGL), and Cushing syndrome (CS). Although relatively uncommon, these conditions confer a disproportionately high cardiovascular risk that extends beyond blood pressure elevation. Aldosterone, catecholamines, and cortisol each induce myocardial fibrosis, oxidative stress, and endothelial dysfunction, leading to left ventricular hypertrophy (LVH), arrhythmias, and heart failure. In PA, chronic aldosterone excess activates mineralocorticoid receptors in cardiac and vascular tissues, promoting collagen deposition, diastolic dysfunction, and atrial fibrillation (AF) that may regress after adrenalectomy or pharmacologic blockade. PPGL causes episodic catecholamine surges resulting in β-adrenergic overstimulation, calcium overload, and microvascular ischemia, producing reversible or sometimes persistent catecholamine-induced cardiotoxicity. CS induces concentric hypertrophy, metabolic derangements, and vascular injury through prolonged glucocorticoid exposure, with cardiovascular recovery often incomplete after biochemical remission. Despite distinct hormonal origins, these disorders share convergent mechanisms, including fibroblast activation, mitochondrial injury, and maladaptive remodeling, that define endocrine cardiomyopathy. Early detection and targeted hormonal treatment can reverse much of the cardiac and vascular damage, whereas delayed recognition leads to irreversible fibrosis and persistent diastolic dysfunction. Recognition of these hormone-specific mechanisms is crucial for clinicians to anticipate, manage, and prevent these deleterious cardiovascular effects. Advances in molecular genetics, cardiac imaging, and biomarker research are improving our understanding of genotype-phenotype relationships and long-term reversibility of injury. Endocrine HT should therefore be recognized as a systemic cardiovascular disorder in which hormonal excess functions as a primary pathogenic driver; timely diagnosis and multidisciplinary care remain key to reducing morbidity and mortality.

Keywords

primary aldosteronism, pheochromocytoma, Cushing syndrome, endocrine hypertension, cardiovascular remodeling

Introduction

Endocrine hypertension (HT) represents a distinct and clinically significant form of secondary HT in which excessive hormonal secretion leads to persistent blood pressure elevation and direct cardiovascular injury. Among its causes, primary aldosteronism (PA), pheochromocytoma and paraganglioma (PPGL), and Cushing syndrome (CS) are the most relevant due to their well-established associations with structural and functional cardiac abnormalities [1]. Although uncommon compared to essential HT, these conditions are crucial to identify because the resulting cardiovascular damage often exceeds that expected from elevated blood pressure alone.

PA is now recognized as the most frequent endocrine cause of HT, occurring in approximately 5–10% of all hypertensive patients and up to 20% of those with resistant HT [2, 3]. Aldosterone excess contributes not only to volume expansion and hypokalemia but also to myocardial fibrosis and diastolic dysfunction through mineralocorticoid receptor activation within the heart and vasculature [3, 4]. Patients with PA exhibit higher rates of atrial fibrillation (AF), left ventricular hypertrophy (LVH), and heart failure compared with patients with essential HT of similar severity [5].

PPGLs are catecholamine-producing neuroendocrine tumors arising from chromaffin cells of the adrenal medulla or extra-adrenal paraganglia. They cause episodic or sustained sympathetic activation through excessive secretion of epinephrine, norepinephrine, or dopamine. Surges in circulating catecholamines can precipitate severe HT, arrhythmias, and cardiomyopathy, often mimicking acute coronary syndromes [6]. The cardiovascular manifestations are typically reversible once the tumor is removed, but delayed recognition can result in irreversible structural damage.

CS, though less common, exemplifies the cardiovascular toxicity of chronic cortisol excess. Cortisol stimulates mineralocorticoid receptors, increases vascular sensitivity to catecholamines, and promotes insulin resistance and central obesity, creating a high-risk metabolic and hemodynamic profile [7]. Even after biochemical remission, many patients demonstrate residual cardiac remodeling, suggesting that prolonged exposure produces partially irreversible effects.

Despite differing hormonal origins, these disorders converge on shared mechanisms, oxidative stress, endothelial dysfunction, and myocardial fibrosis that ultimately drive adverse cardiac remodeling. Recognizing these mechanisms underscores the importance of distinguishing endocrine HT from essential HT, as its pathogenesis and outcomes differ profoundly [8]. Population-based data indicate that cardiovascular morbidity and mortality are consistently higher in endocrine HT than in essential HT of comparable blood pressure levels. In PA, meta-analyses report two- to threefold higher risks of AF, stroke, coronary artery disease, and heart failure compared with essential HT. Similarly, CS confers a two- to threefold increase in all-cause mortality that may persist despite biochemical remission [8, 9].

This review aims to synthesize current evidence on the cardiac effects of PA, PPGL, and CS, focusing on pathophysiologic mechanisms, clinical manifestations, and the cardiovascular consequences of hormonal excess. By integrating experimental and clinical data, this article seeks to clarify how these distinct endocrine disorders contribute to myocardial injury and to highlight the importance of early recognition and mechanistic understanding in improving cardiovascular outcomes. A comprehensive overview of endocrine forms of HT can be found in the reference textbook Endocrine Hypertension, which provides detailed descriptions of hormonal mechanisms and clinical presentations [10]. The main endocrine causes of HT and their characteristic hormonal profiles are summarized in Table 1.

Table 1. Major endocrine causes of HT and their hormonal profiles.

Disorder	Principal hormone	Source	Mechanism of HT	Biochemical findings	Ref. No.
Primary aldosteronism	Aldosterone	Adrenal cortex (zona glomerulosa)	Sodium retention, potassium loss, plasma volume expansion	↑ Aldosterone, ↓ renin, ↑ ARR	[1–4, 8]
Pheochromocytoma/Paraganglioma	Catecholamines (epinephrine, norepinephrine, dopamine)	Adrenal medulla/extra-adrenal paraganglia	α/β-Adrenergic overstimulation	↑ Plasma/Urinary metanephrines	[6, 23–28]
CS	Cortisol	Adrenal cortex (zona fasciculata)	Mineralocorticoid receptor activation, insulin resistance	↑ Cortisol, loss of diurnal rhythm	[41–44]

ARR: aldosterone-to-renin ratio; HT: hypertension; CS: Cushing syndrome.

Cardiovascular effects of PA

PA is defined by autonomous overproduction of aldosterone, most often due to an aldosterone-producing adenoma or bilateral adrenal hyperplasia. Beyond its renal effects on sodium retention and potassium excretion, excessive aldosterone exerts direct actions on the heart and vasculature that substantially increase cardiovascular morbidity and mortality. Evidence from both experimental and clinical studies has established that PA represents not merely a cause of secondary HT but an independent cardiovascular disease characterized by distinct structural and functional cardiac changes [3, 11].

Structural myocardial remodeling

Aldosterone activates mineralocorticoid receptors in cardiomyocytes, fibroblasts, and vascular smooth muscle cells. This activation triggers oxidative stress, inflammatory cytokine release, and fibrogenic signaling pathways [12, 13]. These effects promote myocardial collagen deposition and hypertrophy, resulting in increased left ventricular stiffness and diastolic dysfunction. Importantly, these processes occur even when blood pressure is comparable to that in essential HT, confirming that aldosterone excess itself has direct myocardial toxicity [14].

Clinical studies have consistently shown that patients with PA have greater left ventricular mass and thicker interventricular septa than those with essential HT. Meta-analyses confirm that these changes persist after adjusting for confounders such as age, duration of HT, and systolic pressure [8]. Cardiac magnetic resonance (CMR) imaging further revealed diffuse interstitial fibrosis in PA, which correlated with reduced left ventricular compliance and impaired strain parameters. These findings demonstrate that structural myocardial remodeling in PA is a hormone-driven process rather than purely a hemodynamic consequence.

Electrical remodeling and arrhythmias

Aldosterone also contributes to atrial remodeling and arrhythmogenesis. Elevated plasma aldosterone levels shorten atrial action potential duration, enhance fibroblast proliferation, and create a substrate for reentry circuits. Epidemiologic data indicate a two- to threefold higher prevalence of AF in PA compared with essential HT [15, 16]. Hypokalemia further destabilizes membrane potentials and amplifies this proarrhythmic effect. Surgical or medical correction of aldosterone excess markedly reduces new-onset AF, confirming a causal link between hyperaldosteronism and atrial disease [17].

In the ventricles, similar fibrotic and electrical alterations lead to impaired relaxation, prolonged QT (interval between Q and T waves on electrocardiogram) intervals, and increased vulnerability to ventricular arrhythmias. Hypokalemia and myocardial fibrosis act synergistically to impair repolarization reserve, predisposing to potentially fatal arrhythmias. Cohort data indicate that patients with PA experience higher rates of heart failure and sudden cardiac death than matched hypertensive controls, independent of blood pressure control [5].

Vascular effects

Aldosterone-induced vascular injury plays an additional role in the cardiovascular phenotype of PA. Activation of mineralocorticoid receptors in endothelial and vascular smooth muscle cells reduces nitric oxide bioavailability, increases oxidative stress, and promotes perivascular inflammation. These mechanisms lead to increased arterial stiffness, impaired flow-mediated dilation, and enhanced atherogenesis [18]. As a result, PA patients exhibit higher carotid intima-media thickness and pulse-wave velocity compared with essential HT, even after adjusting for pressure load.

Importantly, several longitudinal studies have demonstrated that both surgical adrenalectomy and pharmacologic mineralocorticoid receptor blockade can partially reverse cardiac and vascular abnormalities. Regression of LVH, improved diastolic function, and reduced AF burden have been observed within months after treatment [15, 19]. The degree of reversal appears greater after adrenalectomy, likely due to complete hormonal normalization, whereas partial suppression achieved by pharmacologic therapy may not fully mitigate subclinical fibrosis [20]. However, aldosterone-related myocardial fibrosis is often only partially reversible, and structural remodeling may persist even after long-term biochemical remission. In addition, HT associated with PA frequently remains difficult to control or is only partially reversible despite correction of hormonal excess.

Recent molecular discoveries have provided insight into disease heterogeneity within PA. Somatic mutations in *KCNJ5*, *CACNA1D*, and *ATP1A1* genes, identified in aldosterone-producing adenomas, alter calcium signaling and steroidogenesis, contributing to variable aldosterone secretion and clinical severity. Emerging data suggest that patients harboring specific mutations display differing degrees of cardiac remodeling, implying a genotype-phenotype relationship that may ultimately influence cardiovascular risk [3, 21]. An area of ongoing debate concerns the comparative cardiovascular benefits of adrenalectomy versus long-term medical therapy. Evidence suggests that adrenalectomy achieves greater regression of cardiac remodeling and lower arrhythmia incidence, whereas optimized mineralocorticoid receptor antagonist (MRA) therapy may provide comparable outcomes in select patients, particularly those with bilateral disease or high surgical risk [22, 23].

In summary, PA exerts profound cardiovascular effects through mechanisms independent of blood pressure elevation. Excess aldosterone induces myocardial fibrosis, diastolic dysfunction, atrial and ventricular arrhythmias, and vascular injury, all of which contribute to increased cardiovascular morbidity and mortality. These alterations are at least partly reversible following correction of hormonal excess, underscoring the importance of early detection and targeted treatment. Recognition of PA as a systemic cardiovascular disorder rather than a purely adrenal disease has reshaped the understanding of secondary HT and emphasized the need for comprehensive cardiovascular evaluation in affected patients. A comparative overview of the cardiovascular manifestations across PA, pheochromocytoma/paraganglioma, and CS is provided in Table 2.

Table 2. Cardiovascular manifestations of endocrine hypertension.

Features	Primary aldosteronism	Pheochromocytoma/Paraganglioma	CS	Ref. No.
Hypertension pattern	Sustained, often resistant	Paroxysmal or sustained	Sustained, moderate-to-severe	[2, 6, 9, 41]
LV hypertrophy	Common	Variable	Common	[5, 8, 23, 45]
Systolic dysfunction	Rare	Acute (Takotsubo-like)	Present in advanced CS	[24–28, 45]
Diastolic dysfunction	Frequent	Common	Frequent	[3, 5, 46, 49]
Arrhythmias	AF	Ventricular and supraventricular	QT prolongation, AF	[14, 15, 29, 47]

Table 2. Cardiovascular manifestations of endocrine hypertension. (*continued*)

Features	Primary aldosteronism	Pheochromocytoma/Paraganglioma	CS	Ref. No.
Cardiomyopathy	Fibrotic, non-dilated	Catecholamine-induced, reversible	Concentric remodeling	[23, 25, 30, 45]
Vascular pathology	Endothelial dysfunction, arterial stiffness	Vasospasm, microvascular ischemia	Atherosclerosis, stiffness	[17, 23, 48, 50]

AF: atrial fibrillation; CS: Cushing syndrome; LV: left ventricle. QT: interval between Q and T waves on electrocardiogram.

Cardiovascular effects of PPGL

PPGLs are catecholamine-producing neuroendocrine tumors arising from chromaffin cells of the adrenal medulla or extra-adrenal sympathetic and parasympathetic ganglia. Although rare, they represent one of the most dramatic causes of secondary HT due to episodic or sustained secretion of epinephrine, norepinephrine, and dopamine. The cardiovascular manifestations of PPGL extend well beyond blood pressure elevation, encompassing a wide spectrum of structural, electrical, and functional cardiac abnormalities resulting from acute and chronic catecholamine excess [6, 24].

Structural myocardial remodeling

Excessive catecholamine release produces intense α- and β-adrenergic receptor stimulation, leading to marked vasoconstriction, tachycardia, and increased myocardial oxygen demand. Sustained exposure causes direct myocardial toxicity mediated by oxidative stress, calcium overload, and mitochondrial dysfunction [25]. The resulting histopathologic pattern, characterized by myofibrillar degeneration, contraction band necrosis, and interstitial fibrosis, is considered the hallmark of catecholamine-induced cardiomyopathy. These histopathologic findings correspond to the clinical spectrum of catecholamine-induced cardiomyopathy, ranging from transient myocardial stunning to fulminant heart failure. These lesions can develop even in the absence of coronary artery disease and are often reversible after tumor removal, highlighting their functional rather than ischemic nature [26]. Recent studies have confirmed that catecholamine-induced cardiomyopathy results from β-adrenergic overstimulation, calcium overload, oxidative stress, and mitochondrial injury, which together lead to reversible or, when prolonged, irreversible myocardial damage [27, 28].

Clinically, PPGL can present with a broad range of cardiac manifestations. Some patients experience transient myocardial ischemia, while others develop acute heart failure or cardiogenic shock. The condition frequently mimics acute coronary syndrome, with elevated troponin levels and electrocardiographic changes suggestive of infarction despite normal coronary angiography. Echocardiographic findings often reveal global or segmental left ventricular dysfunction resembling Takotsubo (stress-induced) cardiomyopathy. The catecholamine surge induces apical or midventricular ballooning through β-adrenergic overstimulation and direct cytotoxicity [29].

Electrical remodeling and arrhythmias

Arrhythmias are also common in PPGL and may be life-threatening. Excess catecholamines increase automaticity, shorten repolarization, and precipitate both supraventricular and ventricular tachyarrhythmias. QT interval prolongation, often observed in these patients, further predisposes them to torsades de pointes. Sudden cardiac death may occur during hypertensive crises triggered by stress, anesthesia, or certain medications that stimulate tumor secretion [30]. Early recognition and preoperative adrenergic blockade are therefore essential to prevent catastrophic cardiovascular events. Catecholamine excess prolongs the QT interval and induces afterdepolarizations, explaining the occurrence of polymorphic ventricular tachycardia and sudden cardiac death reported in pheochromocytoma crises. Persistent fibrosis may sustain arrhythmic risk even after biochemical remission [31, 32].

Chronic catecholamine exposure leads to structural remodeling and persistent diastolic dysfunction. Even after tumor resection, some patients exhibit residual hypertrophy and fibrosis, likely reflecting long-term subclinical injury. Imaging studies using CMR demonstrate increased extracellular volume and late

gadolinium enhancement consistent with diffuse interstitial fibrosis. Histologic studies confirm that fibrosis is mainly perivascular and patchy, corresponding to areas of contraction band necrosis [33].

The severity of cardiac involvement appears to correlate with tumor phenotype and catecholamine profile. Norepinephrine-predominant tumors, typically of extra-adrenal origin, are associated with sustained HT and concentric LVH, while epinephrine-dominant tumors are more likely to cause paroxysmal crises and acute myocardial stunning. Dopamine-secreting paragangliomas may produce little or no HT but still exert cardiotoxic effects through oxidative stress and endothelial injury [34]. Genetic background also influences cardiovascular risk. Mutations in succinate dehydrogenase subunit B (SDHB) and other mitochondrial genes are associated with higher catecholamine output and increased incidence of cardiomyopathy compared with sporadic or succinate dehydrogenase subunit D (SDHD)-related cases [24, 35].

Vascular effects

Excess catecholamine exposure in PPGL produces profound vascular dysfunction. Continuous α-adrenergic receptor stimulation causes intense vasoconstriction, increased systemic vascular resistance, and endothelial injury. These effects impair nitric oxide bioavailability and promote oxidative stress, leading to loss of vasodilatory capacity. Chronic exposure induces structural vascular remodeling characterized by medial hypertrophy, perivascular fibrosis, and increased arterial stiffness. Repeated catecholamine surges may also precipitate coronary vasospasm and microvascular ischemia, contributing to myocardial injury even in the absence of epicardial coronary disease. Over time, this combination of endothelial dysfunction, inflammation, and structural remodeling establishes a substrate for persistent HT and long-term cardiovascular risk even after tumor removal [24]. In addition to macrovascular vasospasm, catecholamine-driven microvascular dysfunction contributes to subendocardial ischemia and cardiomyocyte necrosis. These microcirculatory disturbances are increasingly recognized as key contributors to stress-induced cardiomyopathy associated with pheochromocytoma [36].

Following surgical removal of the tumor, most patients experience rapid normalization of blood pressure and significant improvement in cardiac function within weeks to months. In cases with severe preoperative cardiac dysfunction, there is often marked functional recovery; however, residual fibrosis and persistent diastolic dysfunction may remain, particularly when diagnosis or treatment is delayed [37]. Long-term follow-up remains essential, as some patients may later develop heart failure with preserved ejection fraction (EF) or recurrent arrhythmias even after achieving biochemical cure [38]. The persistence of arrhythmic risk after biochemical cure remains an area of ongoing debate. Although cardiac function usually normalizes, residual myocardial fibrosis and electrical remodeling may contribute to late arrhythmogenic events in a subset of patients, underscoring the importance of continued rhythm surveillance during long-term follow-up [39].

From a mechanistic standpoint, catecholamine excess acts through multiple pathways. β1-Adrenergic overstimulation increases intracellular calcium and cyclic AMP, leading to myocyte necrosis and apoptosis. Reactive oxygen species generated during catecholamine metabolism exacerbate mitochondrial injury, while α-adrenergic-mediated vasoconstriction produces microvascular ischemia. The combination of these factors disrupts myocardial energy homeostasis and promotes fibrosis. Inflammatory cytokine upregulation further amplifies tissue damage, creating a self-perpetuating cycle of injury [25, 31].

In summary, PPGL causes diverse and potentially severe cardiac complications through catecholamine-mediated toxic, metabolic, and microvascular mechanisms. Excessive β-adrenergic stimulation leads to calcium overload, oxidative stress, mitochondrial dysfunction, and microvascular ischemia, resulting in reversible catecholamine-induced cardiomyopathy or Takotsubo-like myocardial stunning [40, 41]. Prompt diagnosis, adequate preoperative adrenergic blockade, and timely surgical resection are critical to prevent irreversible cardiac damage. Recognizing the cardiac manifestations of PPGL is essential, as they often represent the first clinical clue to an otherwise occult endocrine tumor and carry major prognostic implications.

Cardiovascular effects of CS

CS is characterized by chronic exposure to excess glucocorticoids, either from endogenous overproduction or exogenous administration. Endogenous CS most commonly results from an adrenocorticotropic hormone (ACTH)-secreting pituitary adenoma, adrenal adenoma or carcinoma, or ectopic ACTH secretion. Regardless of etiology, sustained cortisol excess induces profound cardiovascular and metabolic disturbances that make CS one of the most lethal endocrine disorders if left untreated [42, 43]. The cardiovascular phenotype of CS is distinguished by systemic HT, central obesity, insulin resistance, dyslipidemia, endothelial dysfunction, and atherosclerosis, collectively creating a high-risk profile for premature cardiovascular morbidity and mortality [44].

Cortisol affects the cardiovascular system through multiple interrelated mechanisms. At the molecular level, glucocorticoids bind to both glucocorticoid and mineralocorticoid receptors, with the latter contributing to sodium retention, plasma volume expansion, and increased systemic vascular resistance [4]. Cortisol also potentiates the vasoconstrictive effects of catecholamines and angiotensin II by upregulating adrenergic receptors and impairing nitric oxide bioavailability [45]. Endothelial dysfunction develops early, marked by reduced vasodilatory capacity and increased oxidative stress. Chronic exposure further promotes vascular remodeling and stiffness, explaining the high prevalence of HT in CS, reported in up to 80% of patients [9, 42].

Structural myocardial remodeling

At the myocardial level, prolonged glucocorticoid excess induces concentric LVH, interstitial fibrosis, and diastolic dysfunction. Histologic analyses show mild or absent myocardial fibrosis in most patients, indicating that glucocorticoid excess primarily causes hypertrophy rather than fibrotic remodeling. Unlike aldosterone excess, glucocorticoid-related cardiac changes are largely reversible, and HT usually improves after biochemical remission. CMR studies confirm increased left ventricular mass and reduced strain, correlating with the duration and severity of hypercortisolism [9]. In experimental models, cortisol exposure impairs calcium handling and mitochondrial function, contributing to contractile dysfunction and decreased myocardial efficiency.

Beyond structural changes, CS profoundly alters metabolic and inflammatory homeostasis. Cortisol enhances hepatic gluconeogenesis, decreases peripheral glucose uptake, and induces insulin resistance, leading to hyperglycemia and diabetes mellitus in up to half of affected patients [44]. Dyslipidemia, particularly elevated triglycerides and low high-density-lipoprotein (HDL) cholesterol, further accelerates atherogenesis. These metabolic derangements, combined with endothelial injury, explain the increased prevalence of coronary artery disease and stroke observed in Cushing cohorts [46]. Inflammatory mediators, including interleukin-6 and tumor necrosis factor-alpha, remain elevated even after biochemical remission, contributing to persistent vascular risk.

Electrical remodeling and arrhythmias

Atrial and ventricular arrhythmias have also been described in CS, likely related to myocardial fibrosis, hypokalemia, and altered repolarization. Prolonged QT intervals and increased sympathetic activity have been documented and may account for cases of sudden cardiac death reported in uncontrolled hypercortisolism [47]. Although overt systolic dysfunction is uncommon, chronic diastolic impairment can progress to heart failure with preserved EF if hypercortisolism persists.

Vascular effects

Chronic cortisol excess in CS profoundly alters vascular structure and function. Glucocorticoids enhance vasoconstrictor sensitivity to catecholamines and angiotensin II while suppressing endothelial nitric oxide synthase, leading to reduced nitric oxide bioavailability and endothelial dysfunction. Sustained exposure promotes oxidative stress, inflammation, and vascular smooth muscle hypertrophy, resulting in increased arterial stiffness and impaired flow-mediated dilation. Cortisol also accelerates atherogenesis by inducing dyslipidemia, insulin resistance, and low-grade inflammation. Histopathologic studies demonstrate intimal

thickening and perivascular collagen deposition, reflecting both metabolic and hemodynamic injury. Even after biochemical remission, partial persistence of endothelial dysfunction and arterial stiffness has been observed, indicating that prolonged hypercortisolism may cause irreversible vascular remodeling and sustained cardiovascular risk [48].

Treatment of the underlying hypercortisolism, surgical, medical, or radiotherapeutic, leads to significant cardiovascular improvement, but complete reversal of cardiac and vascular damage is not always achieved, as many patients continue to exhibit residual diastolic dysfunction or features of metabolic syndrome after biochemical remission. Several studies show regression of LVH and partial normalization of endothelial function after remission; however, residual diastolic dysfunction and metabolic abnormalities may persist for years [49, 50]. These findings indicate that cardiovascular injury in CS is only partially reversible and emphasize the importance of early diagnosis and intervention before irreversible structural remodeling occurs.

Subclinical or mild autonomous cortisol secretion, increasingly recognized in patients with adrenal incidentalomas, also carries measurable cardiovascular risk. Even modest cortisol excess without overt clinical features is associated with increased arterial stiffness, insulin resistance, and higher rates of cardiovascular events compared with non-functioning adrenal tumors [51]. These data suggest a continuum of cortisol-related cardiovascular toxicity extending from mild biochemical hypercortisolism to overt CS. However, the management of subclinical CS remains an area of ongoing debate. While adrenalectomy may improve metabolic and cardiovascular outcomes in selected patients with autonomous cortisol secretion, many experts recommend conservative management and close follow-up for individuals with mild biochemical abnormalities or elevated surgical risk. Current guidelines emphasize individualized assessment based on the degree of cortisol autonomy and comorbid burden [52, 53].

Similar to subclinical CS, milder or subclinical variants of other endocrine causes of HT have also been described. In PA, 'nonclassic' or normokalemic forms with intermittently elevated aldosterone-renin ratios may contribute to subtle cardiac remodeling and endothelial dysfunction. Likewise, biochemically mild or 'silent' pheochromocytomas can induce transient HT, myocardial strain, or arrhythmic events through intermittent catecholamine secretion. Recognition of these subclinical phenotypes is clinically relevant, as even modest hormonal excess can predispose to cardiovascular remodeling and warrants closer monitoring [54, 55].

In summary, chronic cortisol excess produces multifactorial cardiovascular injury involving mineralocorticoid receptor activation, endothelial dysfunction, myocardial fibrosis, and profound metabolic derangements. The persistence of cardiovascular risk after biochemical remission underscores the irreversible nature of prolonged glucocorticoid exposure. Recognition of these mechanisms is essential for comprehensive management and long-term follow-up of patients with CS, who remain vulnerable to cardiovascular complications even after apparent endocrine cure. The key molecular and cellular mechanisms through which hormonal excess leads to myocardial and vascular injury are summarized in Table 3.

Table 3. Pathophysiologic mechanisms linking hormonal excess to cardiac injury.

Mechanistic pathway	PA	PPGL	CS	Common outcome	Ref. No.
Mineralocorticoid receptor activation	+++	–	++	Fibrosis, hypertrophy	[3, 4, 11, 12, 41]
β-Adrenergic overstimulation	–	+++	+/–	Myocyte necrosis, arrhythmia	[23–28, 47]
Oxidative stress	++	+++	++	Mitochondrial damage	[11, 12, 24, 30, 44]
Endothelial dysfunction	++	++	+++	Arterial stiffness	[17, 23, 48, 50]
Inflammation and cytokine activation	++	++	+++	Fibrosis, remodeling	[11, 12, 24, 43, 46]

In CS, β-adrenergic overstimulation is primarily indirect, resulting from cortisol-induced upregulation of adrenergic receptors and enhanced sympathetic sensitivity. –: denotes absence or negligible contribution; +/–: denotes weak or indirect involvement; +: denotes mild involvement; ++: denotes moderate involvement; +++: denotes strong and well-established involvement. PA: primary aldosteronism; PPGL: pheochromocytoma and paraganglioma; CS: Cushing syndrome.

Diagnosis of endocrine HT

Accurate diagnosis and tailored management of endocrine HT are essential to prevent irreversible cardiovascular damage. Because the cardiac manifestations of hormonal excess often precede overt endocrine symptoms, clinicians must maintain a high index of suspicion in patients with resistant or atypical HT, hypokalemia, or hypertensive crises accompanied by arrhythmia or heart failure [1, 8]. Early biochemical screening and appropriate localization studies enable targeted therapy and significantly improve cardiac outcomes.

The diagnostic approach should begin with recognition of clinical patterns suggestive of hormonal etiology. In suspected PA, the plasma aldosterone-to-renin ratio (ARR) remains the cornerstone of screening. Testing should be performed under standardized conditions, ideally after withdrawal of interfering medications such as MRAs and diuretics. A high ARR, confirmed by suppression testing, establishes biochemical evidence of autonomous aldosterone production [1]. Subsequent adrenal imaging by computed tomography helps exclude large or malignant lesions, while adrenal venous sampling distinguishes unilateral from bilateral disease, information critical for therapeutic planning [2].

For PPGL, biochemical confirmation relies on measurement of plasma-free or urinary fractionated metanephrines, which provide the highest sensitivity for catecholamine-secreting tumors. Positive results should prompt localization with cross-sectional imaging (computed tomography or magnetic resonance imaging). Functional imaging with 123I-metaiodobenzylguanidine (MIBG) scintigraphy or positron emission tomography (PET) using 18F-fluorodopa or 68Ga-DOTATATE further delineates tumor distribution and metastatic potential [25]. Genetic testing is now recommended for all PPGL patients, as up to 40% harbor germline mutations (SDHB, SDHD, VHL, RET, etc.) that influence prognosis and follow-up strategies [6].

Evaluation for CS requires biochemical evidence of cortisol excess. Initial screening includes the 1 mg overnight dexamethasone suppression test, late-night salivary cortisol, or 24-h urinary free cortisol measurement [43]. Once hypercortisolism is confirmed, ACTH determination differentiates ACTH-dependent from independent causes. Pituitary magnetic resonance imaging or adrenal computed tomography is then used for localization. Because cardiovascular risk increases even in mild or subclinical cortisol excess, clinicians should consider testing in patients with unexplained metabolic syndrome, osteoporosis, or early-onset HT [42].

Recent advances in cardiac imaging have expanded the diagnostic assessment of endocrine HT beyond conventional echocardiography. CMR with T1 mapping enables early detection of diffuse myocardial fibrosis and tissue remodeling before overt systolic dysfunction develops. Speckle-tracking echocardiography allows quantification of subclinical left ventricular strain abnormalities, providing a sensitive marker of early myocardial involvement. Additionally, PET and hybrid imaging modalities can identify microvascular dysfunction and metabolic alterations related to hormonal excess. Incorporating these tools into routine evaluation may facilitate earlier recognition of reversible myocardial injury and improve risk stratification in endocrine HT [56, 57].

Management and therapeutic strategies

Management strategies are guided by etiology, hormonal activity, and cardiovascular status. In PA, treatment is determined by laterality: unilateral disease is treated with laparoscopic adrenalectomy, while bilateral adrenal hyperplasia requires long-term medical therapy with MRAs such as spironolactone or eplerenone. Early targeted therapy helps reverse LVH and reduce arrhythmic burden [19]. Beyond traditional steroidal MRAs, newer non-steroidal agents such as finerenone and esaxerenone have shown greater receptor selectivity and improved safety profiles with reduced incidence of hyperkalemia and endocrine side effects. Recent trials suggest that these agents may attenuate myocardial fibrosis, reduce LVH, and lower cardiovascular event rates in patients with PA or resistant HT. Although data remain limited, their integration into therapeutic algorithms represents a promising step toward more targeted cardiovascular protection in aldosterone-mediated disease [58–60].

For PPGL, definitive therapy is surgical resection following meticulous preoperative preparation. Adequate α-adrenergic blockade with agents like phenoxybenzamine or doxazosin is mandatory to prevent intraoperative hypertensive crises; β-blockers are added only after α-blockade to control tachyarrhythmia. Cardiac function should be reassessed postoperatively, as most patients demonstrate marked recovery of ventricular performance [37].

In CS, surgical removal of the causative lesion, transsphenoidal resection for pituitary adenoma or adrenalectomy for adrenal tumors, remains first-line treatment. When surgery is not feasible or hypercortisolism persists, medical therapies such as steroidogenesis inhibitors (ketoconazole, metyrapone, osilodrostat) or glucocorticoid receptor antagonists (mifepristone) are employed. Medical therapy with steroidogenesis inhibitors may be used preoperatively to control hypercortisolism or in patients who are not surgical candidates. In many patients, postoperative glucocorticoid replacement is also required until hypothalamic-pituitary-adrenal axis recovery occurs. Blood pressure and metabolic parameters often improve with cortisol normalization, though some degree of cardiac remodeling may remain [44]. Patients with subclinical CS benefit from individualized management balancing surgical risk against cardiovascular benefit.

Because the cardiovascular consequences of endocrine HT frequently persist even after biochemical cure, comprehensive postoperative follow-up is essential. Serial echocardiography, ambulatory blood pressure monitoring, and metabolic profiling allow detection of residual organ damage. Continued use of renin-angiotensin-aldosterone system inhibitors or MRAs may be indicated in cases of incomplete hormonal suppression or irreversible myocardial fibrosis [61]. In addition, lifelong screening for recurrence or contralateral disease is required in both PA and PPGL, particularly in hereditary or bilateral cases.

Optimal management requires close collaboration among endocrinologists, cardiologists, radiologists, and surgeons. Such a multidisciplinary model ensures accurate diagnosis, safe perioperative care, and systematic evaluation of cardiac recovery. The increasing integration of molecular diagnostics, minimally invasive surgical techniques, and advanced imaging has markedly improved both survival and quality of life in endocrine HT. However, gaps remain in understanding the long-term reversibility of cardiac injury and in defining which patients benefit most from early surgical versus medical approaches. Future clinical trials focusing on cardiovascular endpoints rather than biochemical remission alone will be key to optimizing care and preventing residual heart disease in this high-risk population. An overview of treatment strategies and their cardiovascular effects across the three disorders is presented in Table 4.

Table 4. Therapeutic strategies and cardiovascular outcomes.

Disorder	Primary treatment	Adjunctive therapy	Cardiac effects after treatment	Reversibility	Ref. No.
Primary aldosteronism	Adrenalectomy (unilateral)/MRA therapy (bilateral)	MRA therapy	↓ LV mass, ↓ AF incidence	Partial to near-complete	[2, 18–22]
Pheochromocytoma/Paraganglioma	Preoperative α/β-blockade + surgical resection	α-Blockade ± β-blockade preop	Recovery of EF, resolution of cardiomyopathy	Often marked, but residual fibrosis is possible	[23, 28, 30, 36, 37]
CS	Pre & post-operative steroidogenesis inhibitors + surgical resection of the source	Postoperative glucocorticoid replacement	Regression of LVH, partial improvement in diastolic function	Partial	[41, 45, 48–50]

AF: atrial fibrillation; EF: ejection fraction; LV: left ventricle; LVH: left ventricular hypertrophy; MRA: mineralocorticoid receptor antagonist; CS: Cushing syndrome.

Future perspectives

Endocrine HT provides a natural human model linking hormonal dysregulation with cardiovascular injury. Although its molecular pathways are increasingly defined, major questions remain regarding the determinants of irreversible myocardial damage and the mechanisms of incomplete recovery after hormonal correction. Long-term observational studies show that despite normalization of blood pressure and endocrine function, subtle abnormalities in diastolic relaxation, endothelial function, and arrhythmic risk often persist. These findings emphasize the need for early recognition, continuous follow-up, and a mechanistic understanding of endocrine-mediated cardiac remodeling [61].

Future research should prioritize biomarker discovery to detect subclinical cardiac injury before overt structural changes occur. Circulating markers of fibrosis, oxidative stress, and mitochondrial dysfunction could improve risk stratification and therapeutic monitoring. Similarly, advanced cardiac imaging, including myocardial strain analysis and T1 mapping, may help identify reversible stages of endocrine cardiomyopathy and assess treatment response. Integration of imaging biomarkers with hormonal and genetic data could redefine disease classification and guide individualized care [62, 63].

At the molecular level, genomic and transcriptomic profiling of aldosterone-producing adenomas, catecholamine-secreting tumors, and cortisol-producing lesions is expected to elucidate genotype-phenotype relationships that influence cardiovascular outcomes. Understanding how specific mutations alter hormonal output and myocardial susceptibility may lead to precision-targeted therapies that extend beyond endocrine control to direct myocardial protection [64, 65].

Finally, interdisciplinary collaboration between endocrinology and cardiology will be critical. Multicenter prospective trials focusing on cardiovascular endpoints, not only biochemical remission, are needed to define long-term outcomes and optimize treatment timing. The convergence of molecular medicine, advanced imaging, and hormonal therapeutics holds the potential to transform the management of endocrine HT from reactive blood pressure control to proactive cardiovascular preservation [66, 67].

Conclusions

Endocrine forms of HT, including PA, PPGL, and CS, represent distinct but pathophysiologically convergent causes of cardiovascular disease. Each disorder induces specific biochemical and structural abnormalities, yet they share common pathways leading to myocardial remodeling, fibrosis, endothelial dysfunction, and arrhythmogenesis. Collectively, they exemplify how hormonal excess acts as an independent and potent determinant of cardiovascular morbidity and mortality, beyond the contribution of systemic blood pressure itself. Across large cohort and registry studies, the risk of major adverse cardiovascular events and all-cause mortality is roughly two- to fourfold higher in endocrine HT than in essential HT, underscoring its distinct clinical impact.

Timely diagnosis and targeted treatment can significantly reverse structural and functional cardiac alterations, particularly when initiated before irreversible fibrosis develops. Surgical or medical correction of the hormonal source leads to substantial improvement in left ventricular mass, diastolic function, and arrhythmic burden; however, delayed diagnosis or prolonged hormonal exposure often results in persistent subclinical dysfunction and residual cardiovascular risk. Even after biochemical remission, continued surveillance remains necessary to detect late complications such as heart failure with preserved EF or recurrent arrhythmias.

Viewing endocrine HT as a primary cardiovascular disorder rather than merely a secondary form of HT reframes its clinical importance. Its recognition underscores the need for routine endocrine evaluation in resistant or atypical HT, disproportionate organ damage, or unexplained arrhythmia. Multidisciplinary management, uniting endocrinology, cardiology, imaging, and molecular science, is essential to improve early detection, optimize treatment strategies, and prevent irreversible cardiac injury.

Ultimately, integrating mechanistic understanding with clinical practice will help translate hormonal and molecular discoveries into tangible cardiovascular protection. Early identification and individualized therapy offer the best chance to reduce morbidity, prevent heart failure progression, and improve long-term survival in patients with endocrine HT.

Abbreviations

ACTH: adrenocorticotropic hormone

AF: atrial fibrillation

ARR: aldosterone-to-renin ratio

CMR: cardiac magnetic resonance

CS: Cushing syndrome

EF: ejection fraction

HDL: high-density-lipoprotein

HT: hypertension

LV: left ventricle

LVH: left ventricular hypertrophy

MIBG: metaiodobenzylguanidine

MRA: mineralocorticoid receptor antagonist

PA: primary aldosteronism

PET: positron emission tomography

PPGL: pheochromocytoma and paraganglioma

SDHB: succinate dehydrogenase subunit B

SDHD: succinate dehydrogenase subunit D

Declarations

Author contributions

MMŞ: Conceptualization, Investigation, Writing—original draft. MK: Conceptualization, Writing—review & editing. MY: Writing—review & editing. MCÇ: Conceptualization, Investigation, Writing—original draft. LB: Supervision, Validation. YK: Supervision, Validation. All authors read and approved the submitted version.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

Not applicable.

Funding

No financial funding was received for this study.

Publisher's note

Open Exploration maintains a neutral stance on jurisdictional claims in published institutional affiliations and maps. All opinions expressed in this article are the personal views of the author(s) and do not represent the stance of the editorial team or the publisher.

References

1. Carey RM, Calhoun DA, Bakris GL, Brook RD, Daugherty SL, Dennison-Himmelfarb CR, et al.; American Heart Association Professional/Public Education and Publications Committee of the Council on Hypertension; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Genomic and Precision Medicine; Council on Peripheral Vascular Disease; Council on Quality of Care and Outcomes Research; Stroke Council. Resistant Hypertension: Detection, Evaluation, and Management: A Scientific Statement From the American Heart Association. Hypertension. 2018;72: e53–90. [DOI] [PubMed] [PMC]
2. Reincke M, Bancos I, Mulatero P, Scholl UI, Stowasser M, Williams TA. Diagnosis and treatment of primary aldosteronism. Lancet Diabetes Endocrinol. 2021;9:876–92. [DOI] [PubMed]
3. Funder JW, Carey RM, Mantero F, Murad MH, Reincke M, Shibata H, et al. The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2016;101:1889–916. [DOI] [PubMed]
4. Buonafine M, Bonnard B, Jaisser F. Mineralocorticoid Receptor and Cardiovascular Disease. Am J Hypertens. 2018;31:1165–74. [DOI] [PubMed]
5. Hundemer GL, Curhan GC, Yozamp N, Wang M, Vaidya A. Cardiometabolic outcomes and mortality in medically treated primary aldosteronism: a retrospective cohort study. Lancet Diabetes Endocrinol. 2018;6:51–9. [DOI] [PubMed] [PMC]
6. Lenders JW, Duh QY, Eisenhofer G, Gimenez-Roqueplo AP, Grebe SK, Murad MH, et al.; Endocrine Society. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2014;99:1915–42. [DOI] [PubMed]
7. Fallo F, Di Dalmazi G, Beuschlein F, Biermasz NR, Castinetti F, Elenkova A, et al. Diagnosis and management of hypertension in patients with Cushing's syndrome: a position statement and consensus of the Working Group on Endocrine Hypertension of the European Society of Hypertension. J Hypertens. 2022;40:2085–101. [DOI] [PubMed]
8. Monticone S, D'Ascenzo F, Moretti C, Williams TA, Veglio F, Gaita F, et al. Cardiovascular events and target organ damage in primary aldosteronism compared with essential hypertension: a systematic review and meta-analysis. Lancet Diabetes Endocrinol. 2018;6:41–50. [DOI] [PubMed]
9. Dekkers OM, Horváth-Puhó E, Jørgensen JO, Cannegieter SC, Ehrenstein V, Vandenbroucke JP, et al. Multisystem morbidity and mortality in Cushing's syndrome: a cohort study. J Clin Endocrinol Metab. 2013;98:2277–84. [DOI] [PubMed]
10. Pappachan JM, Fernandez CJ, editors. Endocrine Hypertension: From Basic Science to Clinical Practice. Academic Press; 2023. [DOI]
11. Young WF Jr. Diagnosis and treatment of primary aldosteronism: practical clinical perspectives. J Intern Med. 2019;285:126–48. [DOI] [PubMed]
12. Chilton RJ, Silva-Cardoso J. Mineralocorticoid receptor antagonists in cardiovascular translational biology. Cardiovasc Endocrinol Metab. 2023;12:e0289. [DOI] [PubMed] [PMC]

13. Rocha R, Rudolph AE, Frierdich GE, Nachowiak DA, Kekec BK, Blomme EA, et al. Aldosterone induces a vascular inflammatory phenotype in the rat heart. Am J Physiol Heart Circ Physiol. 2002;283: H1802–10. [DOI] [PubMed]
14. Brilla CG, Matsubara LS, Weber KT. Antifibrotic effects of spironolactone in preventing myocardial fibrosis in systemic arterial hypertension. Am J Cardiol. 1993;71:12A–6A. [DOI] [PubMed]
15. Milliez P, Girerd X, Plouin PF, Blacher J, Safar ME, Mourad JJ. Evidence for an increased rate of cardiovascular events in patients with primary aldosteronism. J Am Coll Cardiol. 2005;45:1243–8. [DOI] [PubMed]
16. Pan CT, Liao CW, Tsai CH, Chen ZW, Chen L, Hung CS, et al.; TAIPAI study group. Influence of Different Treatment Strategies on New-Onset Atrial Fibrillation Among Patients With Primary Aldosteronism: A Nationwide Longitudinal Cohort-Based Study. J Am Heart Assoc. 2020;9:e013699. [DOI] [PubMed] [PMC]
17. Rossi GP, Maiolino G, Flego A, Belfiore A, Bernini G, Fabris B, et al.; PAPY Study Investigators. Adrenalectomy Lowers Incident Atrial Fibrillation in Primary Aldosteronism Patients at Long Term. Hypertension. 2018;71:585–91. [DOI] [PubMed]
18. Nishimoto K, Seki T, Hayashi Y, Mikami S, Al-Eyd G, Nakagawa K, et al. Human Adrenocortical Remodeling Leading to Aldosterone-Producing Cell Cluster Generation. Int J Endocrinol. 2016;2016: 7834356. [DOI] [PubMed] [PMC]
19. Catena C, Colussi G, Lapenna R, Nadalini E, Chiuch A, Gianfagna P, et al. Long-term cardiac effects of adrenalectomy or mineralocorticoid antagonists in patients with primary aldosteronism. Hypertension. 2007;50:911–8. [DOI] [PubMed]
20. Chen SY, Chen JY, Huang WC, Puar THK, Chin Kek P, Chueh JS, et al. Cardiovascular outcomes and all-cause mortality in primary aldosteronism after adrenalectomy or mineralocorticoid receptor antagonist treatment: a meta-analysis. Eur J Endocrinol. 2022;187:S47–58. [DOI] [PubMed]
21. Fernandes-Rosa FL, Williams TA, Riester A, Steichen O, Beuschlein F, Boulkroun S, et al. Genetic spectrum and clinical correlates of somatic mutations in aldosterone-producing adenoma. Hypertension. 2014;64:354–61. [DOI] [PubMed]
22. Marzano L, Zoccatelli F, Pizzolo F, Friso S. Adrenalectomy Versus Medical Therapy in Primary Aldosteronism: A Meta-Analysis of Long-Term Cardiac Remodeling and Function: Medical versus Adrenalectomy Treatment Compared in Hyperaldosteronism (MATCH) Study. Hypertension. 2025;82: e142–53. [DOI] [PubMed]
23. Nayak SS, Amini-Salehi E, Joukar F, Biswas P, Nobakht S, Letafatkar N, et al. Cardiovascular and all-cause mortality outcomes of adrenalectomy versus medical treatment in primary aldosteronism: an umbrella review. Int J Surg. 2024;110:7367–80. [DOI] [PubMed] [PMC]
24. Petrák O, Krátká Z, Holaj R, Zítek M, Nguyen Nikrýnová T, Klímová J, et al. Cardiovascular Complications in Pheochromocytoma and Paraganglioma: Does Phenotype Matter? Hypertension. 2024;81:595–603. [DOI] [PubMed]
25. Kassim TA, Clarke DD, Mai VQ, Clyde PW, Mohamed Shakir KM. Catecholamine-induced cardiomyopathy. Endocr Pract. 2008;14:1137–49. [DOI] [PubMed]
26. Y-Hassan S, Falhammar H. Cardiovascular Manifestations and Complications of Pheochromocytomas and Paragangliomas. J Clin Med. 2020;9:2435. [DOI] [PubMed] [PMC]
27. Nazari MA, Hasan R, Haigney M, Maghsoudi A, Lenders JWM, Carey RM, et al. Catecholamine-induced hypertensive crises: current insights and management. Lancet Diabetes Endocrinol. 2023;11:942–54. [DOI] [PubMed]
28. Nazari MA, Rosenblum JS, Haigney MC, Rosing DR, Pacak K. Pathophysiology and Acute Management of Tachyarrhythmias in Pheochromocytoma: JACC Review Topic of the Week. J Am Coll Cardiol. 2020; 76:451–64. [DOI] [PubMed] [PMC]
29. Agarwal V, Kant G, Hans N, Messerli FH. Takotsubo-like cardiomyopathy in pheochromocytoma. Int J Cardiol. 2011;153:241–8. [DOI] [PubMed]

30. Menke-van der Houven van Oordt CW, Twickler TB, van Asperdt FG, Ackermans P, Timmers HJ, Hermus AR. Pheochromocytoma mimicking an acute myocardial infarction. Neth Heart J. 2007;15:248–51. [DOI] [PubMed] [PMC]
31. Bansal R, Dhirawani B, Rathi C, Lokhandwala Y. Pheochromocytoma presenting with recurrent syncope, prolonged QT interval and macroscopic T-wave alternans. Ann Pediatr Cardiol. 2024;17:455–8. [DOI] [PubMed] [PMC]
32. Saavedra T JS, Nati-Castillo HA, Valderrama Cometa LA, Rivera-Martínez WA, Asprilla J, Castaño-Giraldo CM, et al. Pheochromocytoma: an updated scoping review from clinical presentation to management and treatment. Front Endocrinol (Lausanne). 2024;15:1433582. [DOI] [PubMed] [PMC]
33. Li G, Xu S, Shi S, Ouyang X, Mai P, Zhang H, et al. Acute myocardial injury induced by pheochromocytoma: a case report. BMC Cardiovasc Disord. 2025;25:682. [DOI] [PubMed] [PMC]
34. Timmers HJLM, Taïeb D, Pacak K, Lenders JWM. Imaging of Pheochromocytomas and Paragangliomas. Endocr Rev. 2024;45:414–34. [DOI] [PubMed] [PMC]
35. Cascón A, Calsina B, Monteagudo M, Mellid S, Díaz-Talavera A, Currás-Freixes M, et al. Genetic bases of pheochromocytoma and paraganglioma. J Mol Endocrinol. 2023;70:e220167. [DOI] [PubMed]
36. Garrison PG, East L, Wanna C, Paudel B, Tallaj J, McElwee S, et al. Pheochromocytoma-Induced Cardiomyopathy Requiring Mechanical Circulatory Support With Cardiac Recovery Following Surgical Resection. JACC Case Rep. 2025;30:104564. [DOI] [PubMed] [PMC]
37. Torresan F, Beber A, Schiavone D, Zovato S, Galuppini F, Crimì F, et al. Long-Term Outcomes after Surgery for Pheochromocytoma and Sympathetic Paraganglioma. Cancers (Basel). 2023;15:2890. [DOI] [PubMed] [PMC]
38. Zelinka T, Petrák O, Turková H, Holaj R, Strauch B, Kršek M, et al. High incidence of cardiovascular complications in pheochromocytoma. Horm Metab Res. 2012;44:379–84. [DOI] [PubMed]
39. Guo N, Liu T, Zhao P, Bai S. Long-Term Cardiovascular Complications in Patients With Pheochromocytomas and Paragangliomas After Surgery: A Large Multi-Center Study. Clin Endocrinol (Oxf). 2025;102:273–80. [DOI] [PubMed]
40. Çoner A, Özyıldız AG. Pheochromocytoma: An overlooked reversible cause of heart failure with reduced ejection fraction. Turk Kardiyol Dern Ars. 2021;49:501–5. [DOI] [PubMed]
41. Crawford RM, Anderson EJ. Not 'Inactive' After All: Cardiotoxic Mechanisms of Catecholamine Metabolism by Monoamine Oxidase. Cardiovasc Toxicol. 2025;25:1202–21. [DOI] [PubMed] [PMC]
42. Cicala MV, Mantero F. Hypertension in Cushing's syndrome: from pathogenesis to treatment. Neuroendocrinology. 2010;92 Suppl 1:44–9. [DOI] [PubMed]
43. Nieman LK, Biller BM, Findling JW, Murad MH, Newell-Price J, Savage MO, et al.; Endocrine Society. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015;100:2807–31. [DOI] [PubMed] [PMC]
44. Pivonello R, Isidori AM, De Martino MC, Newell-Price J, Biller BM, Colao A. Complications of Cushing's syndrome: state of the art. Lancet Diabetes Endocrinol. 2016;4:611–29. [DOI] [PubMed]
45. Whitworth JA, Williamson PM, Mangos G, Kelly JJ. Cardiovascular consequences of cortisol excess. Vasc Health Risk Manag. 2005;1:291–9. [DOI] [PubMed] [PMC]
46. Muiesan ML, Lupia M, Salvetti M, Grigoletto C, Sonino N, Boscaro M, et al. Left ventricular structural and functional characteristics in Cushing's syndrome. J Am Coll Cardiol. 2003;41:2275–9. [DOI] [PubMed]
47. Colao A, Pivonello R, Spiezia S, Faggiano A, Ferone D, Filippella M, et al. Persistence of increased cardiovascular risk in patients with Cushing's disease after five years of successful cure. J Clin Endocrinol Metab. 1999;84:2664–72. [DOI] [PubMed]
48. Faggiano A, Pivonello R, Spiezia S, De Martino MC, Filippella M, Di Somma C, et al. Cardiovascular risk factors and common carotid artery caliber and stiffness in patients with Cushing's disease during active disease and 1 year after disease remission. J Clin Endocrinol Metab. 2003;88:2527–33. [DOI] [PubMed]

49. Hacioglu A, Firat ST, Caglar AS, Karaca Z, Kalay N, Taheri S, et al. Cardiovascular evaluation and endothelial dysfunction in Cushing syndrome following remission: a prospective study. J Endocrinol Invest. 2024;47:645–53. [DOI] [PubMed]
50. Frustaci A, Letizia C, Verardo R, Grande C, Petramala L, Russo MA, et al. Cushing Syndrome Cardiomyopathy: Clinicopathologic Impact of Cortisol Normalization. Circ Cardiovasc Imaging. 2016; 9:e004569. [DOI] [PubMed]
51. Mazziotti G, Gazzaruso C, Giustina A. Diabetes in Cushing syndrome: basic and clinical aspects. Trends Endocrinol Metab. 2011;22:499–506. [DOI] [PubMed]
52. Terzolo M, Pia A, Reimondo G. Subclinical Cushing's syndrome: definition and management. Clin Endocrinol (Oxf). 2012;76:12–8. [DOI] [PubMed]
53. Khadembashiri MM, Mohseni S, Harandi H, Pejman Sani M, Khadembashiri MA, Atlasi R, et al. Comparison of adrenalectomy with conservative treatment on mild autonomous cortisol secretion: a systematic review and meta-analysis. Front Endocrinol (Lausanne). 2024;15:1374711. [DOI] [PubMed] [PMC]
54. Fassnacht M, Tsagarakis S, Terzolo M, Tabarin A, Sahdev A, Newell-Price J, et al. European Society of Endocrinology clinical practice guidelines on the management of adrenal incidentalomas, in collaboration with the European Network for the Study of Adrenal Tumors. Eur J Endocrinol. 2023; 189:G1–42. [DOI] [PubMed]
55. Constantinescu G, Preda C, Constantinescu V, Siepmann T, Bornstein SR, Lenders JWM, et al. Silent pheochromocytoma and paraganglioma: Systematic review and proposed definitions for standardized terminology. Front Endocrinol (Lausanne). 2022;13:1021420. [DOI] [PubMed] [PMC]
56. Brown JM, Robinson-Cohen C, Luque-Fernandez MA, Allison MA, Baudrand R, Ix JH, et al. The Spectrum of Subclinical Primary Aldosteronism and Incident Hypertension: A Cohort Study. Ann Intern Med. 2017;167:630–41. [DOI] [PubMed] [PMC]
57. Chen Y, Xu T, Xu J, Zhu L, Wang D, Li Y, et al. Strain Imaging for the Early Detection of Cardiac Remodeling and Dysfunction in Primary Aldosteronism. Diagnostics (Basel). 2022;12:543. [DOI] [PubMed] [PMC]
58. Wu T, Ren Y, Wang W, Cheng W, Zhou F, He S, et al. Left Ventricular Remodeling in Patients with Primary Aldosteronism: A Prospective Cardiac Magnetic Resonance Imaging Study. Korean J Radiol. 2021;22:1619–27. [DOI] [PubMed] [PMC]
59. Ito S, Itoh H, Rakugi H, Okuda Y, Yoshimura M, Yamakawa S. Double-Blind Randomized Phase 3 Study Comparing Esaxerenone (CS-3150) and Eplerenone in Patients With Essential Hypertension (ESAX-HTN Study). Hypertension. 2020;75:51–8. [DOI] [PubMed]
60. Bakris GL, Agarwal R, Anker SD, Pitt B, Ruilope LM, Rossing P, et al.; FIDELIO-DKD Investigators. Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes. N Engl J Med. 2020;383: 2219–29. [DOI] [PubMed]
61. Hundemer GL, Curhan GC, Yozamp N, Wang M, Vaidya A. Renal Outcomes in Medically and Surgically Treated Primary Aldosteronism. Hypertension. 2018;72:658–66. [DOI] [PubMed] [PMC]
62. Fernandes-Rosa FL, Boulkroun S, Fedlaoui B, Hureaux M, Travers-Allard S, Drossart T, et al. New advances in endocrine hypertension: from genes to biomarkers. Kidney Int. 2023;103:485–500. [DOI] [PubMed]
63. Gasior T. Advances in Cardiac Imaging and Genetic Testing for Diagnosis and Risk Stratification in Cardiomyopathies: 2024 Update. J Clin Med. 2024;13:7166. [DOI] [PubMed] [PMC]
64. Sade LE, Hazirolan T, Kozan H, Ozdemir H, Hayran M, Eroglu S, et al. T1 Mapping by Cardiac Magnetic Resonance and Multidimensional Speckle-Tracking Strain by Echocardiography for the Detection of Acute Cellular Rejection in Cardiac Allograft Recipients. JACC Cardiovasc Imaging. 2019;12:1601–14. [DOI] [PubMed]
65. Dahia PL. Pheochromocytoma and paraganglioma pathogenesis: learning from genetic heterogeneity. Nat Rev Cancer. 2014;14:108–19. [DOI] [PubMed]

66. Nanba K, Omata K, Else T, Beck PCC, Nanba AT, Turcu AF, et al. Targeted Molecular Characterization of Aldosterone-Producing Adenomas in White Americans. J Clin Endocrinol Metab. 2018;103:3869–76. [DOI] [PubMed] [PMC]
67. Fernandez CJ, Nagendra L, Alkhalifah M, Pappachan JM. Endocrine Hypertension: The Urgent Need for Greater Global Awareness. touchREV Endocrinol. 2023;19:31–41. [DOI] [PubMed] [PMC]