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Normotensive Primary Aldosteronism – Does it Exist?

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Keywords
hyperaldosteronism, RAAS, normotension, aldosterone-producing cell cluster, subclinical hyperaldosteronism

received 24.10.2024
accepted after revision 23.01.2025

Bibliography
Horm Metab Res 2025; 57: 149–155
DOI 10.1055/a-2530-1792
ISSN 0018-5043

Georg Thieme Verlag KG, Oswald-Hesse-Straße 50, 70469 Stuttgart, Germany

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ABSTRACT

Heightened aldosterone levels are associated with increased risk of renal sequelae, cardiovascular morbidity and mortality. Historically, primary aldosteronism is linked to hypertension. However, growing evidence reveals its presence even in normotensive individuals. This review consolidates data from diverse sources, delves into clinical studies of this underexplored condition, discusses the potential mechanisms, and provides a comprehensive and an up-to-date overview of the current state of knowledge. It highlights the evidence and understanding of normotensive primary aldosteronism, summarizes findings, and identifies opportunities for future research in this area. By addressing the clinical evidence, risk of hypertension development and possible mechanisms involved, this review aims to advance the understanding of this distinct form of primary aldosteronism and inspire further research in this emerging field.

Introduction

Primary aldosteronism (PA) is increasingly known as the most common cause of secondary hypertension, accounting for up to 20 % among patients with resistant hypertension [1]. Traditionally, it has been associated with hypertension and spontaneous hypokalemia, characterized by elevated aldosterone and suppressed renin. However, most patients with PA present with normokalemia. Elevated aldosterone has been demonstrated to be deleterious as it induces inflammation and increases oxidative stress, resulting in a multitude of cardio-metabolic disorders [2–4], ultimately leading to increased cardiovascular morbidity and mortality [5]. The Endocrine Society guidelines recommend screening for PA in individuals with high likelihood of this disorder, such as those with sustained blood pressure (BP) above 150/100 mmHg, drug-resistant hypertension, and hypertension accompanied by hypokalemia or adrenal incidentaloma [6]. From these criteria, hypertension appears to be a hallmark of PA, and the absence of hypertension is often thought to negate the need for PA screening.

Nevertheless, since the first description of normotensive PA in 1972 [7], several cases have been reported, challenging the traditional understanding that PA is exclusive to hypertensive individuals. While current guidelines advise screening for PA in patients with sustained BP above 150/100 mmHg, emerging evidence indicates that PA can occur even in patients with stage 1 hypertension and in normotensive individuals.

This condition has predominantly been reported among middle-aged Eurasians and Japanese females [8]. Given that patients with elevated aldosterone levels are at a higher risk of cardiovascular, metabolic, and renal complications compared to those with essential hypertension of similar severity, normotensive PA becomes an interesting entity, suggesting a potential continuous spectrum of autonomous aldosterone secretion and mineralocorticoid activity, spanning from normotensive to overtly hypertensive. Hence, this review aims to explore the evolving landscape of PA, offering insights into the mechanisms underlying this condition and its clinical implications.