

# Isolated Systolic Hypertension in Geriatrics

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## Abstract

Hypertension, often called the “silent killer”, is a major risk factor for heart attacks and strokes in the elderly. Its effective management is crucial to prevent damage to the heart, brain, and kidneys. Isolated systolic hypertension (ISH) is particularly critical in the elderly population. Cardiovascular risk factors, including pulse pressure and wave velocity, are closely associated with systolic blood pressure and influenced by arterial stiffness and wave reflections. Managing ISH is complex due to the potential negative effects of certain medications and individual variability in treatment response. This paper will address these issues, evaluating antihypertensive drugs, combination therapy, personalized treatment plans, and updated guidelines for managing ISH.

## Keywords

Hypertension, Geriatric or Elderly or Adults, Types of Hypertension, Tests, First-Line Treatment, Drugs, Isolated Systolic Hypertension, Other Diseases

## 1. Introduction

Hypertension, commonly known as high blood pressure, is a significant risk factor for cardiovascular events such as heart attacks and strokes, particularly in the elderly population [1]-[3]. Isolated Systolic Hypertension (ISH) is the most prevalent form of hypertension in older adults, characterized by a systolic blood pressure (SBP) of 140 mm Hg or higher and a diastolic blood pressure (DBP) of less than 90 mm Hg [4] [5]. The condition primarily arises due to the decreased elasticity of the arterial system, an inevitable consequence of aging [6] [7]. According to the 2017 American College of Cardiology/American Heart Association Blood Pressure Guidelines, an SBP of 130 mm Hg is now classified as hypertensive at any age [8].

### 1.1. Research Background

Hypertension is often referred to as a “silent killer” because it typically presents

no symptoms until significant damage has occurred [9]. Effective management of hypertension is crucial to reduce the risk of heart, brain, and kidney damage [10]. This involves vigilant therapy, regular follow-up, and lifestyle adjustments such as a nutritious diet, regular exercise, and avoiding smoking and excessive alcohol use [11]. Despite these measures, ISH remains a critical cardiovascular disease in elderly individuals, influenced by factors such as enhanced arterial stiffness and premature wave reflections [4] [5].

## 1.2. Previous Research and Existing Problems

Previous research has extensively studied the impact of various antihypertensive therapies on cardiovascular outcomes. However, concerns have been raised about the potential negative effects of certain medications, such as beta-blockers and diuretics, on other cardiovascular risk factors like blood lipids and glucose metabolism [12] [13]. Traditional beta-blockers, for instance, have been associated with an increased risk of diabetes, although newer, vasodilating beta-blockers have a more favorable metabolic profile [14] [15]. Additionally, the variability in individual responses to antihypertensive therapy, influenced by genetic factors, comorbidities, and other medications, complicates the management of ISH [16].

## 1.3. Problems Addressed in This Paper

This paper aims to address several key issues in the management of ISH in the elderly:

**Evaluation of Antihypertensive Therapies:** Assess the efficacy and safety of various antihypertensive drugs, including newer agents with better metabolic profiles.

**Combination Therapy:** Explore the role and benefits of combination therapy in managing ISH, particularly in patients with complex comorbidities.

**Personalized Treatment Plans:** Highlight the importance of personalized treatment plans that consider genetic factors, comorbidities, and other medications to optimize efficacy and minimize adverse effects.

**Monitoring and Management:** Discuss the need for regular monitoring of renal function and electrolyte levels to prevent complications associated with antihypertensive therapy.

**Implications of Updated Guidelines:** Analyze the implications of the 2017 ACC/AHA guidelines for the diagnosis and management of ISH in older adults, considering their increased risk for adverse outcomes at lower blood pressure thresholds.

## 2. Types of Hypertensions

Listed below are six types of hypertension with comprehensive overviews of each. Each type of hypertension has unique characteristics, causes, and management strategies. Primary hypertension is the most common and is influenced by

various lifestyle and genetic factors. Secondary hypertension results from other medical conditions and requires treating the underlying cause. Malignant hypertension is a medical emergency with severe consequences if not treated promptly, leading to acute organ damage and requiring immediate medical intervention.

Isolated Systolic Hypertension (ISH) is prevalent in the elderly due to arterial stiffness and requires a combination of lifestyle modifications and medications to manage. White Coat Hypertension occurs when blood pressure readings are elevated in a clinical setting but normal at home, often due to anxiety, and is managed through regular monitoring and stress management techniques. Resistant Hypertension is high blood pressure that remains uncontrolled despite the use of three or more antihypertensive medications, necessitating a thorough evaluation for secondary causes and optimization of treatment regimens.

Understanding these distinctions is crucial for healthcare providers to develop effective, personalized treatment plans. Regular monitoring, lifestyle modifications, and adherence to prescribed treatments are essential components of managing all types of hypertension. Early detection and intervention are key to improving outcomes and preventing long-term health issues. By addressing the specific characteristics and underlying causes of each type of hypertension, healthcare providers can better manage the condition and reduce the risk of complications.

## 2.1. Primary Hypertension

Primary Hypertension, also known as essential Hypertension, is the most common form of high blood pressure. It has no identifiable cause and is not due to any underlying illnesses, conditions, or disorders. Instead, it results from a combination of genetic, dietary, and lifestyle factors. **Table 1** provides a comprehensive overview of primary hypertension, to include definition, diagnosis, causes and risk factors, pathophysiology, symptoms, complications, diagnosis methods, management and treatment, and prognosis and prevention [17]-[21].

**Table 1.** Comprehensive overview primary hypertension.

Aspect	Details
<b>Definition</b>	Primary hypertension, also known as essential hypertension, is high blood pressure with no identifiable secondary cause.
<b>Diagnosis</b>	Blood pressure consistently exceeding 130/80 mm Hg.
<b>Causes and Risk Factors</b>	<ul style="list-style-type: none"> <li>- <b>Genetics:</b> Family history of hypertension.</li> <li>- <b>Age:</b> Increased risk with age, especially after 65.</li> <li>- <b>Diet:</b> High salt intake, excessive alcohol, high saturated fats.</li> <li>- <b>Obesity:</b> Excess body weight.</li> <li>- <b>Physical Inactivity:</b> Sedentary lifestyle.</li> <li>- <b>Stress:</b> Chronic stress.</li> <li>- <b>Other Factors:</b> Conditions like diabetes and sleep apnea.</li> </ul>

## Continued

<b>Pathophysiology</b>	<ul style="list-style-type: none"> <li>- <b>Increased Peripheral Resistance:</b> Narrowing of small arteries and arterioles.</li> <li>- <b>Increased Cardiac Output:</b> Related to increased blood volume or heart rate.</li> <li>- <b>Renal Sodium Retention:</b> Increased blood volume.</li> <li>- <b>Sympathetic Nervous System Overactivity:</b> Vasoconstriction and increased heart rate.</li> <li>- <b>Hormonal Factors:</b> Renin-angiotensin-aldosterone system.</li> </ul>
<b>Symptoms</b>	Often asymptomatic (“silent killer”). When present: headaches, dizziness, shortness of breath, nosebleeds, blurred vision, chest pain.
<b>Complications</b>	<ul style="list-style-type: none"> <li>- <b>Heart Disease:</b> Heart attack, heart failure, left ventricular hypertrophy.</li> <li>- <b>Stroke:</b> Damage to brain blood vessels.</li> <li>- <b>Kidney Disease:</b> Damage to kidney blood vessels.</li> <li>- <b>Vision Loss:</b> Damage to eye blood vessels.</li> <li>- <b>Aneurysms:</b> Abnormal artery bulges.</li> </ul>
<b>Diagnosis Methods</b>	<ul style="list-style-type: none"> <li>- <b>Blood Pressure Measurement:</b> Multiple occasions.</li> <li>- <b>Medical History and Physical Examination:</b> Identify risk factors and rule out secondary causes.</li> <li>- <b>Laboratory Tests:</b> Blood tests, urine tests, imaging studies.</li> </ul>
<b>Management and Treatment</b>	<ul style="list-style-type: none"> <li>- <b>Lifestyle Modifications:</b></li> <li>- <b>Diet:</b> Heart-healthy diet (e.g., DASH diet).</li> <li>- <b>Exercise:</b> Regular physical activity.</li> <li>- <b>Weight Loss:</b> Maintain healthy weight.</li> <li>- <b>Limiting Alcohol:</b> Reduce intake.</li> <li>- <b>Reducing Sodium Intake:</b> Limit salt.</li> <li>- <b>Stress Management:</b> Techniques like meditation, yoga.</li> <li>- <b>Medications:</b></li> <li>- <b>Diuretics:</b> Reduce blood volume.</li> <li>- <b>Beta-Blockers:</b> Reduce heart rate and cardiac output.</li> <li>- <b>ACE Inhibitors:</b> Prevent hormone formation that narrows blood vessels.</li> <li>- <b>ARBs:</b> Block hormone action that narrows blood vessels.</li> <li>- <b>Calcium Channel Blockers:</b> Relax blood vessels.</li> <li>- <b>Others:</b> Alpha-blockers, central agonists, vasodilators.</li> </ul>
<b>Prognosis and Prevention</b>	<ul style="list-style-type: none"> <li>- <b>Prognosis:</b> With proper management, individuals can lead healthy lives.</li> <li>- <b>Prevention:</b> Maintain a healthy lifestyle, regular blood pressure monitoring, adherence to treatments. Early detection and management are crucial.</li> </ul>

## 2.2. Secondary Hypertension:

Secondary Hypertension is less common and occurs due to another medical con-

dition. Unlike primary Hypertension, secondary Hypertension has a specific cause, such as sleep apnea, tumors, or kidney failure. Treating the underlying condition can often reduce or eliminate the high blood pressure. Proper management involves identifying and addressing the root cause of secondary Hypertension. **Table 2** provides a comprehensive overview of Secondary hypertension, to include definition, diagnosis, causes and risk factors, pathophysiology, symptoms, complications, diagnosis methods, management and treatment, and prognosis and prevention [22]-[25].

**Table 2.** Comprehensive overview of secondary hypertension.

Aspect	Details
<b>Definition</b>	Secondary hypertension is high blood pressure caused by another medical condition. It can be due to conditions affecting the kidneys, arteries, heart, or endocrine system.
<b>Diagnosis</b>	Blood pressure consistently exceeding 130/80 mm Hg, with an identifiable secondary cause.
<b>Causes and Risk Factors</b>	<ul style="list-style-type: none"> <li>- <b>Kidney Diseases:</b> Diabetic nephropathy, polycystic kidney disease, glomerular disease, renovascular hypertension.</li> <li>- <b>Endocrine Disorders:</b> Hyperaldosteronism, pheochromocytoma, Cushing syndrome, thyroid disorders.</li> <li>- <b>Cardiovascular Conditions:</b> Coarctation of the aorta.</li> <li>- <b>Sleep Apnea:</b> Obstructive sleep apnea.</li> <li>- <b>Medications:</b> Certain prescription and over-the-counter drugs.</li> <li>- <b>Pregnancy:</b> Conditions like preeclampsia.</li> </ul>
<b>Pathophysiology</b>	<ul style="list-style-type: none"> <li>- <b>Kidney Dysfunction:</b> Impaired kidney function leads to fluid retention and increased blood pressure.</li> <li>- <b>Hormonal Imbalances:</b> Excessive production of hormones like aldosterone, cortisol, or catecholamines.</li> <li>- <b>Vascular Abnormalities:</b> Narrowing of arteries (e.g., renal artery stenosis) increases blood pressure.</li> <li>- <b>Sleep Apnea:</b> Repeated episodes of low oxygen during sleep increase blood pressure.</li> </ul>
<b>Symptoms</b>	Often asymptomatic. When present: severe or resistant hypertension, very high blood pressure (systolic >180 mm Hg or diastolic >120 mm Hg), sudden-onset hypertension, hypertension not responding to medication, no family history of hypertension, no obesity.
<b>Complications</b>	<ul style="list-style-type: none"> <li>- <b>Heart Disease:</b> Heart attack, heart failure.</li> <li>- <b>Stroke:</b> Due to damage to brain blood vessels.</li> <li>- <b>Kidney Disease:</b> Progression to chronic kidney disease or kidney failure.</li> <li>- <b>Vision Loss:</b> Damage to eye blood vessels.</li> <li>- <b>Aneurysms:</b> Abnormal artery bulges.</li> </ul>

## Continued

<b>Diagnosis Methods</b>	<ul style="list-style-type: none"> <li>- <b>Blood Pressure Measurement:</b> Multiple occasions.</li> <li>- <b>Medical History and Physical Examination:</b> Identify underlying conditions.</li> <li>- <b>Laboratory Tests:</b> Blood tests, urine tests, imaging studies (e.g., renal ultrasound, CT angiography).</li> </ul>
<b>Management and Treatment</b>	<ul style="list-style-type: none"> <li>- <b>Treat Underlying Condition:</b> Address the primary cause (e.g., surgery for coarctation of the aorta, medication for endocrine disorders).</li> <li>- <b>Lifestyle Modifications:</b></li> <li>- <b>Diet:</b> Heart-healthy diet.</li> <li>- <b>Exercise:</b> Regular physical activity.</li> <li>- <b>Weight Loss:</b> Maintain healthy weight.</li> <li>- <b>Limiting Alcohol:</b> Reduce intake.</li> <li>- <b>Reducing Sodium Intake:</b> Limit salt.</li> <li>- <b>Stress Management:</b> Techniques like meditation, yoga.</li> <li>- <b>Medications:</b></li> <li>- <b>Diuretics:</b> Reduce blood volume.</li> <li>- <b>Beta-Blockers:</b> Reduce heart rate and cardiac output.</li> <li>- <b>ACE Inhibitors:</b> Prevent hormone formation that narrows blood vessels.</li> <li>- <b>ARBs:</b> Block hormone action that narrows blood vessels.</li> <li>- <b>Calcium Channel Blockers:</b> Relax blood vessels.</li> <li>- <b>Others:</b> Alpha-blockers, central agonists, vasodilators.</li> </ul>
<b>Prognosis and Prevention</b>	<ul style="list-style-type: none"> <li>- <b>Prognosis:</b> Depends on the underlying cause and its management.</li> <li>- <b>Prevention:</b> Regular monitoring of blood pressure, managing underlying conditions, maintaining a healthy lifestyle. Early detection and treatment are crucial.</li> </ul>

### 2.3. Malignant Hypertension

Malignant Hypertension is characterized by a sudden and severe increase in blood pressure. Symptoms may include vision issues, extreme fatigue, confusion, anxiety, seizures, and bodily numbness. This condition can be triggered by illnesses such as scleroderma, kidney disease, spinal cord injuries, adrenal gland tumors, cocaine use, and certain medications like birth control pills. Blood pressure typically returns to normal once the underlying issue is resolved. **Table 3** provides a comprehensive overview of Malignant hypertension, to include definition, diagnosis, causes and risk factors, pathophysiology, symptoms, complications, diagnosis methods, management and treatment, and prognosis and prevention [25]-[27].

### 2.4. Isolated Systolic Hypertension (ISH)

ISH is defined by a systolic blood pressure reading greater than 140 mm Hg and a diastolic reading less than 90 mm Hg. **Table 4** provides a comprehensive overview

of Isolated Systolic Hypertension, to include definition, diagnosis, causes and risk factors, pathophysiology, symptoms, complications, diagnosis methods, management and treatment, and prognosis and prevention [28]-[31].

**Table 3.** Comprehensive overview of malignant hypertension.

Aspect	Details
<b>Definition</b>	Malignant hypertension, also known as hypertensive crisis, is a severe form of high blood pressure characterized by a sudden and significant increase in blood pressure, often above 180/120 mm Hg, leading to acute organ damage. It is a medical emergency requiring immediate treatment.
<b>Diagnosis</b>	Blood pressure readings significantly higher than the patient's normal levels, often above 180/120 mm Hg, with signs of acute organ damage.
<b>Causes and Risk Factors</b>	<ul style="list-style-type: none"> <li>- <b>Uncontrolled High Blood Pressure:</b> Primary cause.</li> <li>- <b>Kidney Diseases:</b> Renal artery stenosis, glomerulonephritis.</li> <li>- <b>Endocrine Disorders:</b> Pheochromocytoma, Cushing's syndrome, hyperaldosteronism.</li> <li>- <b>Central Nervous System Disorders:</b> Stroke, brain injury.</li> <li>- <b>Medications and Drugs:</b> Certain prescription drugs, recreational drugs.</li> <li>- <b>Pregnancy:</b> Conditions like preeclampsia.</li> <li>- <b>Other Factors:</b> Autoimmune diseases, severe burns, substance withdrawal.</li> </ul>
<b>Pathophysiology</b>	<ul style="list-style-type: none"> <li>- <b>Vascular Damage:</b> Severe hypertension causes endothelial damage, leading to increased vascular permeability and activation of the coagulation cascade.</li> <li>- <b>Organ Damage:</b> Acute damage to organs such as the heart, kidneys, brain, and eyes due to high blood pressure and vascular injury.</li> <li>- <b>Inflammatory Response:</b> Activation of inflammatory pathways exacerbates tissue damage.</li> </ul>
<b>Symptoms</b>	<ul style="list-style-type: none"> <li>- <b>Neurological:</b> Severe headache, confusion, visual disturbances, seizures.</li> <li>- <b>Cardiovascular:</b> Chest pain, shortness of breath, heart failure.</li> <li>- <b>Renal:</b> Decreased urine output, hematuria.</li> <li>- <b>Gastrointestinal:</b> Nausea, vomiting.</li> <li>- <b>General:</b> Severe anxiety, fatigue, weakness.</li> </ul>
<b>Complications</b>	<ul style="list-style-type: none"> <li>- <b>Heart Disease:</b> Heart attack, heart failure, aortic dissection.</li> <li>- <b>Stroke:</b> Due to damage to brain blood vessels.</li> <li>- <b>Kidney Failure:</b> Acute or chronic kidney injury.</li> <li>- <b>Vision Loss:</b> Damage to eye blood vessels.</li> <li>- <b>Multi-Organ Failure:</b> Due to widespread vascular damage and organ ischemia.</li> </ul>

Continued

<b>Diagnosis Methods</b>	<ul style="list-style-type: none"> <li>- <b>Blood Pressure Measurement:</b> Multiple readings to confirm severe hypertension.</li> <li>- <b>Medical History and Physical Examination:</b> Identify underlying conditions and assess organ damage.</li> <li>- <b>Laboratory Tests:</b> Blood tests, urine tests.</li> <li>- <b>Imaging Studies:</b> Chest X-ray, CT scan, MRI, renal ultrasound.</li> <li>- <b>Electrocardiogram (EKG):</b> To check for heart damage.</li> </ul>
<b>Management and Treatment</b>	<ul style="list-style-type: none"> <li>- <b>Immediate Medical Attention:</b> Hospitalization in an intensive care unit (ICU).</li> <li>- <b>Medications:</b> <ul style="list-style-type: none"> <li>- <b>Intravenous Antihypertensives:</b> Nitroprusside, labetalol, nicardipine to rapidly lower blood pressure.</li> <li>- <b>Oral Antihypertensives:</b> Once blood pressure is stabilized.</li> </ul> </li> <li>- <b>Treat Underlying Cause:</b> Address primary condition causing malignant hypertension.</li> <li>- <b>Supportive Care:</b> Monitoring and managing organ function.</li> </ul>
<b>Prognosis and Prevention</b>	<ul style="list-style-type: none"> <li>- <b>Prognosis:</b> Depends on the promptness of treatment and the extent of organ damage. Early intervention can improve outcomes.</li> <li>- <b>Prevention:</b> Regular monitoring of blood pressure, adherence to antihypertensive medications, managing underlying conditions, maintaining a healthy lifestyle. Early detection and treatment of high blood pressure are crucial.</li> </ul>

**Table 4.** Comprehensive overview of isolated systolic hypertension (ISH).

Aspect	Details
<b>Definition</b>	<p>ISH is defined by a systolic blood pressure (SBP) reading greater than 140 mm Hg and a diastolic blood pressure (DBP) reading less than 90 mm Hg.</p>
<b>Diagnosis</b>	<p>Blood pressure readings consistently showing SBP &gt; 140 mm Hg and DBP &lt; 90 mm Hg.</p>
<b>Causes and Risk Factors</b>	<ul style="list-style-type: none"> <li>- <b>Age:</b> Increased risk with aging due to arterial stiffness.</li> <li>- <b>Arterial Stiffness:</b> Loss of elasticity in large arteries.</li> <li>- <b>Lifestyle Factors:</b> High salt intake, physical inactivity, obesity.</li> <li>- <b>Genetics:</b> Family history of hypertension.</li> <li>- <b>Other Factors:</b> Conditions like diabetes and chronic kidney disease.</li> </ul>
<b>Pathophysiology</b>	<ul style="list-style-type: none"> <li>- <b>Arterial Stiffness:</b> Reduced elasticity of large arteries like the aorta.</li> <li>- <b>Increased Pulse Pressure:</b> Difference between systolic and diastolic pressure increases.</li> <li>- <b>Wave Reflections:</b> Premature return of reflected waves increases systolic pressure.</li> </ul>

## Continued

<b>Symptoms</b>	Often asymptomatic. When present: headaches, dizziness, shortness of breath, chest pain, palpitations.
<b>Complications</b>	<ul style="list-style-type: none"> <li>- <b>Heart Disease:</b> Heart attack, heart failure, left ventricular hypertrophy.</li> <li>- <b>Stroke:</b> Due to damage to brain blood vessels.</li> <li>- <b>Kidney Disease:</b> Progression to chronic kidney disease.</li> <li>- <b>Vision Loss:</b> Damage to eye blood vessels.</li> <li>- <b>Aneurysms:</b> Abnormal artery bulges.</li> </ul>
<b>Diagnosis Methods</b>	<ul style="list-style-type: none"> <li>- <b>Blood Pressure Measurement:</b> Multiple readings to confirm ISH.</li> <li>- <b>Medical History and Physical Examination:</b> Identify risk factors and rule out secondary causes.</li> <li>- <b>Laboratory Tests:</b> Blood tests, urine tests, imaging studies.</li> </ul>
<b>Management and Treatment</b>	<ul style="list-style-type: none"> <li>- <b>Lifestyle Modifications:</b></li> <li>- <b>Diet:</b> Heart-healthy diet (e.g., DASH diet).</li> <li>- <b>Exercise:</b> Regular physical activity.</li> <li>- <b>Weight Loss:</b> Maintain healthy weight.</li> <li>- <b>Limiting Alcohol:</b> Reduce intake.</li> <li>- <b>Reducing Sodium Intake:</b> Limit salt.</li> <li>- <b>Stress Management:</b> Techniques like meditation, yoga.</li> <li>- <b>Medications:</b></li> <li>- <b>Diuretics:</b> Reduce blood volume.</li> <li>- <b>Calcium Channel Blockers:</b> Relax blood vessels.</li> <li>- <b>ACE Inhibitors:</b> Prevent hormone formation that narrows blood vessels.</li> <li>- <b>ARBs:</b> Block hormone action that narrows blood vessels.</li> <li>- <b>Beta-Blockers:</b> Reduce heart rate and cardiac output.</li> <li>- <b>Others:</b> Alpha-blockers, central agonists, vasodilators.</li> </ul>
<b>Prognosis and Prevention</b>	<ul style="list-style-type: none"> <li>- <b>Prognosis:</b> With proper management, individuals can lead healthy lives.</li> <li>- <b>Prevention:</b> Maintain a healthy lifestyle, regular blood pressure monitoring, adherence to treatments. Early detection and management are crucial.</li> </ul>

## 2.5. White Coat Hypertension

This type of Hypertension occurs only when blood pressure is measured in a clinical setting. Outside of medical facilities, blood pressure remains normal. Patients with white coat Hypertension often experience significant anxiety during clinic visits. **Table 5** provides a comprehensive overview of White Coat Hypertension, to include definition, diagnosis, causes and risk factors, pathophysiology, symptoms, complications, diagnosis methods, management and treatment, and prognosis and prevention [32]-[34].

**Table 5.** Comprehensive overview of white coat hypertension.

Aspect	Details
<b>Definition</b>	White coat hypertension occurs when a patient's blood pressure is elevated in a clinical setting but normal at other times.
<b>Diagnosis</b>	Blood pressure readings higher in a clinical setting than at home or in other settings.
<b>Causes and Risk Factors</b>	<ul style="list-style-type: none"> <li>- <b>Anxiety:</b> Increased anxiety or stress in clinical settings.</li> <li>- <b>Previous Experiences:</b> Negative experiences with healthcare.</li> <li>- <b>Personality Traits:</b> Higher levels of anxiety or stress.</li> <li>- <b>Other Factors:</b> Lack of familiarity with clinical environments.</li> </ul>
<b>Pathophysiology</b>	<ul style="list-style-type: none"> <li>- <b>Sympathetic Nervous System Activation:</b> Increased stress and anxiety activate the sympathetic nervous system, raising blood pressure temporarily.</li> </ul>
<b>Symptoms</b>	Typically asymptomatic.
<b>Complications</b>	<ul style="list-style-type: none"> <li>- <b>Misdiagnosis:</b> Risk of being misdiagnosed with chronic hypertension.</li> <li>- <b>Unnecessary Treatment:</b> Potential for unnecessary medication and treatment.</li> <li>- <b>Progression to Sustained Hypertension:</b> Increased risk over time.</li> </ul>
<b>Diagnosis Methods</b>	<ul style="list-style-type: none"> <li>- <b>Ambulatory Blood Pressure Monitoring (ABPM):</b> 24-hour monitoring to compare clinical and home readings.</li> <li>- <b>Home Blood Pressure Monitoring:</b> Regular monitoring at home to compare with clinical readings.</li> </ul>
<b>Management and Treatment</b>	<ul style="list-style-type: none"> <li>- <b>Lifestyle Modifications:</b></li> <li>- <b>Diet:</b> Heart-healthy diet.</li> <li>- <b>Exercise:</b> Regular physical activity.</li> <li>- <b>Stress Management:</b> Techniques like meditation, yoga.</li> <li>- <b>Regular Monitoring:</b> Frequent blood pressure checks at home.</li> <li>- <b>Education and Reassurance:</b> Informing patients about the condition to reduce anxiety.</li> </ul>
<b>Prognosis and Prevention</b>	<ul style="list-style-type: none"> <li>- <b>Prognosis:</b> Generally good if managed properly.</li> <li>- <b>Prevention:</b> Regular monitoring, stress management, and maintaining a healthy lifestyle.</li> </ul>

## 2.6. Resistant Hypertension

Resistant Hypertension is high blood pressure that remains uncontrolled despite treatment with three or more antihypertensive medications, including a diuretic. It affects approximately 1% - 15% of people with Hypertension and is associated with a higher risk of cardiovascular disease, stroke, and kidney damage. Treatment may involve additional medications or procedures, along with lifestyle modifications such as weight loss and increased physical activity. **Table 6** provides a comprehensive overview of Resistant Hypertension, to include definition, diagnosis, causes and risk factors, pathophysiology, symptoms, complications, diagnosis methods, management and treatment, and prognosis and prevention [35]-[37].

**Table 6.** A comprehensive overview of resistant hypertension.

Aspect	Details
<b>Definition</b>	Resistant hypertension is high blood pressure that remains uncontrolled despite treatment with three or more antihypertensive medications, including a diuretic.
<b>Diagnosis</b>	Blood pressure consistently exceeding 130/80 mm Hg despite treatment with three or more antihypertensive medications, including a diuretic.
<b>Causes and Risk Factors</b>	<ul style="list-style-type: none"> <li>- <b>Secondary Hypertension:</b> Underlying conditions like kidney disease, endocrine disorders.</li> <li>- <b>Medication Nonadherence:</b> Not taking medications as prescribed.</li> <li>- <b>Lifestyle Factors:</b> High salt intake, obesity, physical inactivity.</li> <li>- <b>Drug Interactions:</b> Medications that interfere with antihypertensive drugs.</li> </ul>
<b>Pathophysiology</b>	<ul style="list-style-type: none"> <li>- <b>Persistent High Blood Pressure:</b> Despite multiple medications, blood pressure remains elevated due to underlying conditions or factors.</li> </ul>
<b>Symptoms</b>	Often asymptomatic. When present: severe or resistant hypertension, very high blood pressure, symptoms related to underlying conditions.
<b>Complications</b>	<ul style="list-style-type: none"> <li>- <b>Heart Disease:</b> Heart attack, heart failure.</li> <li>- <b>Stroke:</b> Due to damage to brain blood vessels.</li> <li>- <b>Kidney Disease:</b> Progression to chronic kidney disease.</li> <li>- <b>Vision Loss:</b> Damage to eye blood vessels.</li> <li>- <b>Aneurysms:</b> Abnormal artery bulges.</li> </ul>
<b>Diagnosis Methods</b>	<ul style="list-style-type: none"> <li>- <b>Blood Pressure Measurement:</b> Multiple readings to confirm resistant hypertension.</li> <li>- <b>Medical History and Physical Examination:</b> Identify underlying conditions and assess medication adherence.</li> <li>- <b>Laboratory Tests:</b> Blood tests, urine tests, imaging studies.</li> </ul>

## Continued

<b>Management and Treatment</b>	<ul style="list-style-type: none"> <li>- <b>Lifestyle Modifications:</b></li> <li>- <b>Diet:</b> Heart-healthy diet.</li> <li>- <b>Exercise:</b> Regular physical activity.</li> <li>- <b>Weight Loss:</b> Maintain healthy weight.</li> <li>- <b>Limiting Alcohol:</b> Reduce intake.</li> <li>- <b>Reducing Sodium Intake:</b> Limit salt.</li> <li>- <b>Stress Management:</b> Techniques like meditation, yoga.</li> <li>- <b>Medications:</b></li> <li>- <b>Optimize Current Medications:</b> Adjust dosages and combinations.</li> <li>- <b>Add Additional Medications:</b> Consider adding aldosterone antagonists, vasodilators.</li> <li>- <b>Treat Underlying Conditions:</b> Address secondary causes of hypertension.</li> </ul>
<b>Prognosis and Prevention</b>	<ul style="list-style-type: none"> <li>- <b>Prognosis:</b> Depends on the underlying cause and its management.</li> <li>- <b>Prevention:</b> Regular monitoring of blood pressure, managing underlying conditions, maintaining a healthy lifestyle. Early detection and treatment are crucial.</li> </ul>

## 2.7. Blood Pressure Ranges

Blood pressure is categorized into different ranges to help diagnose and manage hypertension. Monitoring blood pressure regularly is crucial for early detection and management of hypertension. The following are the general categories [38]:

- **Normal:** SBP < 120 mm Hg and DBP < 80 mm Hg.
- **Elevated:** SBP 120-129 mm Hg and DBP < 80 mm Hg.
- **Hypertension Stage 1:** SBP 130-139 mm Hg or DBP 80 - 89 mm Hg.
- **Hypertension Stage 2:** SBP  $\geq$  140 mm Hg or DBP  $\geq$  90 mm Hg.
- **Hypertensive Crisis:** SBP > 180 mm Hg and/or DBP > 120 mm Hg.

## 2.7. Causes

Hypertension, or high blood pressure, is a chronic condition affecting millions worldwide. It occurs when the force of blood against artery walls is consistently too high, leading to potential damage to blood vessels and organs over time. The causes of hypertension can be broadly categorized into primary and secondary hypertension.

**Primary Hypertension:** Also known as essential hypertension, it has no identifiable cause and is influenced by a combination of genetic, dietary, and lifestyle factors [39].

- **Genetics:** Family history of hypertension.
- **Age:** Increased risk with age.
- **Diet:** High salt intake, excessive alcohol consumption, high saturated fats.
- **Obesity:** Excess body weight.

- **Physical Inactivity:** Sedentary lifestyle.
  - **Stress:** Chronic stress.
  - **Other Factors:** Conditions like diabetes and sleep apnea.
- Secondary Hypertension: Caused by another medical condition.**
- **Kidney Diseases:** Diabetic nephropathy, polycystic kidney disease, glomerular disease, renovascular hypertension.
  - **Endocrine Disorders:** Hyperaldosteronism, pheochromocytoma, Cushing syndrome, thyroid disorders.
  - **Cardiovascular Conditions:** Coarctation of the aorta.
  - **Sleep Apnea:** Obstructive sleep apnea.
  - **Medications:** Certain prescription and over-the-counter drugs.
  - **Pregnancy:** Conditions like preeclampsia.

### 3. Physical Examination for Acute Blood Pressure Measurement

Monitoring blood pressure is essential for maintaining good health. Since normal blood pressure levels can vary from person to person, it is important to reassess them annually. To obtain an accurate reading, follow these steps [40]:

#### 3.1. Rest Before Measurement

The patient should rest for five minutes before taking their blood pressure. This allows the body to relax and dissipate any stress or anxiety. The patient should sit in a chair with both feet flat on the ground and their back straight. This position promotes proper circulation and reduces any extra strain on the body [41].

#### 3.2. Proper Arm Positioning

The patient's arm should be placed on a flat surface at chest or heart level. This positioning ensures that the blood pressure cuff is placed correctly, which is crucial for an accurate reading. Choosing the right cuff size is also important, as an improperly sized cuff can lead to incorrect readings [42].

#### 3.3. Understanding Blood Pressure Components

Blood pressure readings consist of two components: systolic blood pressure (SBP) and diastolic blood pressure (DBP). The SBP is the first Korotkoff sound, which is the sound of blood flow heard when taking a blood pressure reading. The DBP is the fifth Korotkoff sound, which is the point at which the sound of blood flow disappears [43].

#### 3.4. Confirming Hypertension Diagnosis

To confirm a hypertension diagnosis, it is recommended to obtain an average of 2 to 3 blood pressure measurements on two or three separate occasions. This is important because blood pressure can fluctuate throughout the day and may be affected by various factors such as stress, physical activity, and diet [44].

Taking proper blood pressure measurements requires following specific steps and taking measurements on multiple occasions to ensure accuracy. Regular monitoring of blood pressure is crucial for maintaining good health and preventing potential health problems in the future [45].

#### **4. Routine Laboratory and Clinical Investigation**

To evaluate cardiovascular risk and concomitant diseases, several tests should be performed. These tests provide valuable information about a patient's health status and help identify potential risk factors for heart disease and other conditions. Some of the most important tests include:

##### **4.1. 12-Lead Electrocardiographic (ECG) Testing**

This test helps identify various cardiac abnormalities, including left ventricular hypertrophy, atrial dilation, and arrhythmias. Such information is useful in diagnosing and managing various cardiac conditions [46].

##### **4.2. Lipid Panels**

Lipid panels are blood tests that measure various types of lipids, including cholesterol and triglycerides. These tests can be used to calculate a patient's 10-year atherosclerotic cardiovascular disease (ASCVD) risk, helping to identify individuals who may benefit from aggressive risk reduction strategies [47].

##### **4.3. Serum Creatinine Levels**

Serum creatinine levels are important indicators of kidney function. Estimating the glomerular filtration rate (GFR) provides valuable information about a patient's overall health status. These tests are commonly used to assess kidney function and identify individuals at increased risk for kidney disease [48].

##### **4.4. Serum Electrolyte Tests**

These tests provide important information about a patient's electrolyte balance, including levels of sodium and potassium. Imbalances in these electrolytes can have serious health consequences and may require medical intervention [49] [50].

##### **4.5. Thyroid-Stimulating Hormone (TSH) Testing**

TSH testing helps identify individuals with thyroid disorders, which can significantly impact cardiovascular health. Thyroid disorders can increase the risk of heart disease and other health problems [51].

##### **4.6. Urine Analysis**

Urine analysis helps identify a range of health issues, including proteinuria, which is an abnormal amount of protein in the urine. This can be a sign of kidney disease or other health problems [52].

#### 4.7. Urine Microalbuminuria Testing

This specific urine test helps identify individuals at increased risk for kidney disease by measuring the amount of albumin in the urine, an early sign of kidney damage. Performing a range of tests is crucial to evaluate cardiovascular risk and identify potential concomitant diseases. These tests provide valuable information about a patient's overall health status and help identify individuals who may benefit from early intervention and aggressive risk reduction strategies [53].

### 5. Pathophysiology

As people age, their arteries undergo physical changes, such as dilation and stiffening. Elastic arteries, like the aorta, dilate and stiffen with age, reducing their ability to accommodate changes during the cardiac cycle. This arterial stiffness is caused not only by structural changes but also by decreased bioavailability of nitric oxide and vasoactive mediators. High aortic pulse wave velocity (PWV) values are associated with an increased risk of cardiovascular events and mortality. PWV is a strong predictor of future cardiovascular events and all-cause mortality. Elevated blood pressure in the elderly is primarily due to increased arterial stiffness, whereas hypertension in younger patients is typically caused by increased peripheral arterial resistance. Aortic PWV can be estimated noninvasively, and values above 13 m/s are considered elevated [54] [55].

Orthostatic Hypertension is a rare condition where blood pressure significantly increases when moving from a seated or lying position to a standing position. It is believed to be caused by an increase in sympathetic nervous system activity and may be triggered by conditions such as pheochromocytoma, autonomic nervous system disorders, or specific medications. Conversely, orthostatic hypotension is a condition where blood pressure significantly decreases when moving from a seated or lying position to a standing position. This is due to a reduction in baroreflex sensitivity, which usually helps regulate blood pressure during postural changes. Factors such as age, dehydration, certain medications, and underlying medical conditions like Parkinson's disease and diabetes can cause orthostatic hypotension. Adrenergic blockade can prevent orthostatic hypotension by reducing the effects of sympathetic nervous system activity. However, orthostatic hypotension is a side effect of adrenergic blockade that must be monitored, particularly in elderly patients or those with underlying cardiovascular disease. Patients with a history of orthostatic hypotension should have their use of adrenergic blockers closely monitored [56] [57].

Aortic stiffening with age is a common condition affecting large arteries, particularly the aorta, and is linked to an increased risk of cardiovascular disease. This condition is characterized by a decrease in aortic elasticity and compliance, resulting in an increase in systolic blood pressure and a decrease in diastolic blood pressure [54].

## **6. Non-Pharmacological Management of Isolated Systolic Hypertension**

Non-pharmacological interventions play a crucial role in managing isolated systolic hypertension (ISH). Several lifestyle modifications have been shown to effectively lower blood pressure:

### **6.1. DASH Diet**

The Dietary Approaches to Stop Hypertension (DASH) diet has been demonstrated in several clinical trials to lower blood pressure. The DASH-Sodium trial, one of the most well-known studies, examined the impact of different sodium intake levels and the DASH diet on blood pressure in adults with hypertension. The study found that the DASH diet lowers blood pressure by an average of 6/4 mmHg compared to the typical American diet [58].

### **6.2. Regular Physical Activity**

Engaging in regular physical activity can improve cardiovascular health and lower blood pressure levels. Exercise helps to strengthen the heart and improve blood flow, which can reduce the strain on the arteries [59].

### **6.3. Weight Control**

Maintaining a healthy weight is essential for people with hypertension. Weight loss can significantly lower blood pressure and help prevent the condition from worsening [60].

### **6.4. Stress Reduction**

Chronic stress can lead to hypertension. Finding relaxation techniques such as yoga or meditation can be beneficial in managing stress and lowering blood pressure [61].

### **6.5. Limiting Alcohol Intake**

Excessive alcohol consumption can raise blood pressure levels. Limiting alcohol intake is crucial for preventing and managing hypertension [62].

## **7. Pharmacological Management of Isolated Systolic Hypertension: Evidence from Outcome Studies**

Pharmacological interventions are often necessary to manage ISH effectively. Randomized controlled trials have provided evidence for the efficacy of various antihypertensive drugs:

### **7.1. Thiazide-Like Diuretics and Calcium Channel Blockers (CCBs)**

Thiazide-like diuretics and CCBs are effective first-line treatments for ISH. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) concluded that chlorthalidone was more efficient than other antihy-

pertensive drugs, including ACE inhibitors and CCBs, in lowering the risk of stroke, heart failure, and other cardiovascular events in patients with ISH [48].

## 7.2. Calcium Channel Blockers (CCBs)

The Systolic Hypertension in Europe (Syst-Eur) trial found that patients with ISH who received CCB-based treatment had a lower risk of stroke and other cardiovascular events [63].

It is important to note that individual responses to antihypertensive therapy can vary significantly based on genetic factors, comorbidities, and other medications. This variability can impact both efficacy and the risk of adverse effects, emphasizing the need for personalized treatment plans. Additionally, the increasing role and benefits of combination therapy in managing hypertension, especially in patients with ISH, should be considered. Common and effective drug combinations can provide better blood pressure control and reduce the risk of adverse outcomes.

## 8. Evidence from Treatment Trials

For the treatment of hypertension in the elderly, starting with a single-agent oral antihypertensive drug therapy is generally recommended due to the increased risk of orthostatic hypotension in this population. If the initial systolic blood pressure (SBP) is greater than 160 mmHg or the blood pressure is 20/10 mmHg higher than the target blood pressure, treatment with two agents may be necessary to achieve rapid and effective blood pressure control. This is especially important in patients with target organ damage, such as heart failure or chronic kidney disease, who could benefit from more aggressive blood pressure control. The choice of antihypertensive agent should be determined by the individual's comorbidities, medication history, and potential drug-drug interactions and side effects. A diuretic is frequently combined with another antihypertensive agent, such as an ACE inhibitor, ARB, calcium channel blocker, or beta-blocker [61].

### 8.1. Diuretics

Chlorthalidone at doses ranging from 12.5 to 25 mg/day and hydrochlorothiazide at 25 mg/day have been shown to effectively lower blood pressure in ISH patients. However, the optimal dosage of diuretics varies depending on individual patient characteristics and medical history and should be determined by a qualified healthcare provider [16] [49]. The Systolic Hypertension in the Elderly Program (SHEP) study and other trials have demonstrated that thiazide-type diuretics, typically administered in combination with a potassium-sparing diuretic to prevent hypokalemia, significantly lower blood pressure in elderly patients with ISH. The SHEP study found that using a low-dose thiazide-type diuretic (chlorthalidone) alone or in combination with a potassium-sparing diuretic (triamterene) reduced the risk of stroke, heart failure, and coronary heart disease in elderly patients with ISH. Thiazide-type diuretics lower blood pressure by encouraging diuresis and decreasing plasma volume. They can also result in potassium loss, which can cause

hypokalemia, particularly in patients who already have electrolyte problems. Potassium-sparing diuretics such as triamterene or amiloride are frequently used in conjunction with thiazide-type diuretics to avoid hypokalemia. However, there are currently no long-term data available to show whether the addition of a potassium-sparing diuretic affects how well patients with ISH respond to treatment with renin-angiotensin system inhibitors [64]

## **8.2. Beta-Blockers**

Beta-blockers have been relatively ineffective as monotherapy in the treatment of hypertension in the elderly, including patients with ISH. This is because beta-blockers are less effective in lowering systolic blood pressure than other antihypertensive medications such as diuretics and calcium channel blockers. Additionally, elderly patients may have age-related changes in drug metabolism and clearance. Therefore, for elderly patients with hypertension to achieve optimal blood pressure control, beta-blockers may need to be given more frequently or in conjunction with other antihypertensive medications [65]. It is important to specify that traditional, non-vasodilating beta-blockers are more likely to increase the risk of diabetes, whereas newer beta-blockers have a more favorable metabolic profile.

## **8.3. Calcium Channel Blockers (CCBs)**

There is evidence to suggest that CCBs can also directly lessen the stiffness of large conducting arteries, making them especially useful in the treatment of ISH. CCBs work by preventing calcium ions from entering arterial smooth muscle cells, causing the arterial wall to relax and decrease stiffness. This effect is particularly important in patients with ISH, where stiffening of large arteries significantly contributes to increased systolic blood pressure. Furthermore, CCBs are generally well-tolerated and have a low risk of side effects, making them an appropriate choice for elderly hypertensive patients. The use of CCBs should be customized to each patient's unique characteristics and medical background and should be closely monitored by a trained healthcare professional [65]. Dihydropyridine CCBs, such as amlodipine, felodipine, and nifedipine, have consistently demonstrated their efficacy in lowering systolic blood pressure during treatment trials for ISH when used as monotherapy. These drugs work by preventing the entry of calcium ions into the smooth muscle cells of the arteries, causing the arteries to relax and become less stiff, which lowers systolic blood pressure [65].

## **8.4. ACE Inhibitors and Alpha Antagonists**

While some studies have shown that ACE inhibitors only significantly lower blood pressure in the first few hours after administration, other studies have shown that they have a more sustained effect that lasts up to 24 hours or longer [50]. Alpha antagonists, such as terazosin and doxazosin, have shown promising results in lowering SBP in ISH patients. However, since these medications can cause a drop in blood pressure upon standing, the risk of orthostatic hypotension must be care-

fully considered in elderly patients.

### 8.5. Combination Therapy

It has also been demonstrated that labetalol, a combined alpha and beta antagonist, lowers SBP with little side effect in the treatment of ISH. However, it can cause or exacerbate orthostatic hypotension, similar to other medications with antagonistic properties. Although these medications have shown promise in the treatment of ISH, they might not be the first line of treatment due to the potential detrimental consequences in the elderly population. The recommended first-line therapies for ISH continue to be thiazide-type diuretics and calcium channel blockers, with additional medications being considered as second-line alternatives [66].

## 9. Tolerability of Antihypertensive Therapy in ISH

Adverse effects associated with various classes of drugs used to treat isolated systolic hypertension (ISH) have been reported in clinical trials. For example:

- **Diuretics:** Can cause hypokalemia and orthostatic hypotension.
- **Methyldopa:** Can cause sedation and confusion.
- **Dihydropyridine Calcium Antagonists:** Can cause peripheral edema and headache.
- **ACE Inhibitors:** Can cause cough and electrolyte imbalances.

It is important to note that the tolerability of these medications may vary in a larger population of elderly individuals with coexisting cardiovascular, cerebrovascular, and renal dysfunction. The clinical trials often included highly selected patient populations, which may not fully represent the broader elderly population [67]. Additionally, individual responses to antihypertensive therapy can vary significantly based on genetic factors, comorbidities, and other medications, emphasizing the need for personalized treatment plans.

## 10. Noncompliance

Noncompliance with medication regimens is a significant issue in managing hypertension. Several factors contribute to noncompliance, including:

- **Older Age:** Increased forgetfulness or difficulty managing complex regimens.
- **Low Risk of Cardiovascular Events:** Perceived lack of urgency in taking medications.
- **Concurrent Health Issues:** Competing health priorities.
- **Low Socioeconomic Status:** Financial barriers to accessing medications.
- **Complex Medication Regimens:** Difficulty managing multiple medications at various times.
- **Medication Side Effects:** Adverse effects leading to discontinuation.
- **Cost of Medication Regimens:** Financial burden of long-term medication use.

Noncompliance can lead to ineffective blood pressure control, an elevated risk of cardiovascular events, and higher healthcare costs. Strategies to increase medi-

cation adherence include simplifying medication regimens, reducing side effects, educating patients, offering support, and addressing social determinants of health, such as financial barriers to medication access. Healthcare professionals can work with patients to establish reasonable objectives and address any concerns or misunderstandings they might have regarding their medication schedule [68].

## 11. Conclusions and Future Perspectives

There is ongoing debate about which drug should be used first to treat hypertension in elderly patients with ISH. While some authorities recommend thiazide diuretics and beta-blockers as the best first-line drugs based on evidence from outcome studies such as SHEP, others argue that extrapolating findings from these studies to the general population of elderly patients is risky. The presence of co-existing conditions may favor the use of a different class of drug as first-line therapy. Ultimately, the choice of drug should be based on individual patient characteristics such as age, comorbidities, and medication tolerability.

ISH is a significant public health issue, particularly among elderly individuals. Factors such as maleness, being single, older age, lower education levels, and lower income are significant predictors of ISH. The findings suggest that health sector stakeholders should develop preventive strategies for ISH by paying closer attention to these predictive factors. There is ample evidence to support intensive efforts to maintain systolic pressure, as ISH is a significant risk factor for cardiovascular disease and renal illness. Most elderly individuals experience an increase in systolic blood pressure due to decreased flexibility of the conduit arteries. Initial evaluations should include assessing lifestyle factors and identifying concurrent illnesses that affect prognosis and treatment through history, physical examination, and basic laboratory tests.

Future research should focus on personalized treatment plans that consider genetic factors, comorbidities, and other medications to optimize efficacy and minimize adverse effects. Additionally, the role and benefits of combination therapy in managing hypertension, especially in patients with ISH, should be further explored. Monitoring renal function and managing electrolyte imbalances are crucial for patients on antihypertensive therapy. The implications of the 2017 ACC/AHA guidelines for the diagnosis and management of ISH in older adults should also be considered, given their increased risk for adverse outcomes at lower blood pressure thresholds than previously recognized.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

## References

- [1] Fuchs, F.D. and Whelton, P.K. (2020) High Blood Pressure and Cardiovascular Disease. *Hypertension*, **75**, 285-292. <https://doi.org/10.1161/hypertensionaha.119.14240>
- [2] Anisetti, B., Youssef, H., Elkhair, A.M. and Lin, M.P. (2023) Association between

- Within-Visit Blood Pressure Variability, Stroke, Coronary Heart Disease, and Cardiovascular Mortality. *Neurologia i Neurochirurgia Polska*, **57**, 423-429. <https://doi.org/10.5603/pjnns.94839>
- [3] Rios, F.J., Montezano, A.C., Camargo, L.L. and Touyz, R.M. (2023) Impact of Environmental Factors on Hypertension and Associated Cardiovascular Disease. *Canadian Journal of Cardiology*, **39**, 1229-1243. <https://doi.org/10.1016/j.cjca.2023.07.002>
- [4] Thomopoulos, C. (2023) Target Blood Pressure in Isolated Systolic Hypertension: A Meta-Analysis of Randomized Outcome Trials. *Journal of Hypertension*, **41**, 2113-2114. <https://doi.org/10.1097/hjh.0000000000003476>
- [5] Angeli, F., Verdecchia, P., Masnaghetti, S., Vaudo, G. and Reboldi, G. (2020) Treatment Strategies for Isolated Systolic Hypertension in Elderly Patients. *Expert Opinion on Pharmacotherapy*, **21**, 1713-1723. <https://doi.org/10.1080/14656566.2020.1781092>
- [6] Sarnecki, J., Obrycki, Ł., Feber, J., Chełstowska, S., Jurkiewicz, E. and Litwin, M. (2022) Isolated Systolic Hypertension Is Associated with Increased Left Ventricular Mass Index and Aortic Stiffness in Adolescents: A Cardiac Magnetic Resonance Study. *Journal of Hypertension*, **40**, 985-995. <https://doi.org/10.1097/hjh.0000000000003101>
- [7] Espeche, W., Minetto, J., Stavile, N., Cerri, G., C Leiva, S., D, O., *et al.* (2024) Isolated Systolic Hypertension in Young Adults and Its Relationship with Ambulatory Blood Pressure Measurements. *Archives of Clinical Hypertension*, **10**, 1-6. <https://doi.org/10.17352/ach.000034>
- [8] Whelton, P.K. and Carey, R.M. (2018) The 2017 American College of Cardiology/American Heart Association Clinical Practice Guideline for High Blood Pressure in Adults. *JAMA Cardiology*, **3**, 352-353. <https://doi.org/10.1001/jamacardio.2018.0005>
- [9] Zethira, A.T., Hendrati, L., Diyanah, K., Pawitra, A., Jasmine, M., Syahputri, R., *et al.* (2024) Hypertension as a Silent Killer Disease: Education for at-Risk Communities in Pekuwon Village. *Jurnal Layanan Masyarakat (Journal of Public Services)*, **8**, 200-209. <https://doi.org/10.20473/jlm.v8i2.2024.200-209>
- [10] Liao, X., Han, Y., Shen, C., Liu, J. and Wang, Y. (2023) Targeting the NLRP3 Inflammasome for the Treatment of Hypertensive Target Organ Damage: Role of Natural Products and Formulations. *Phytotherapy Research*, **37**, 5622-5638. <https://doi.org/10.1002/ptr.8009>
- [11] Karunarathna, I., Kusumarathna, K., Jayathilaka, P. and Withanage, C. (2024) Comprehensive Management of Hypertension: Strategies, Guidelines, and Emerging Therapies. Uva Clinical Lab.
- [12] Widiarti, W., Saputra, P.B.T., Savitri, C.G., Putranto, J.N.E. and Alkaff, F.F. (2024) The Impact of Cardiovascular Drugs on Hyperglycemia and Diabetes: A Review of 'Unspoken' Side Effects. *Hellenic Journal of Cardiology*. <https://doi.org/10.1016/j.hjc.2024.09.007>
- [13] Haider, R. (2023) Cardiovascular Risk Factors. *Toxicology and Applied Pharmacology Insights*, **6**, 77-87.
- [14] Strauss, M.H., Hall, A.S. and Narkiewicz, K. (2021) The Combination of Beta-Blockers and ACE Inhibitors across the Spectrum of Cardiovascular Diseases. *Cardiovascular Drugs and Therapy*, **37**, 757-770. <https://doi.org/10.1007/s10557-021-07248-1>
- [15] Savage, P.J. (1998) Influence of Long-Term, Low-Dose, Diuretic-Based, Antihypertensive Therapy on Glucose, Lipid, Uric Acid, and Potassium Levels in Older Men

- and Women with Isolated Systolic Hypertension: The Systolic Hypertension in the Elderly Program. *Archives of Internal Medicine*, **158**, 741-751.  
<https://doi.org/10.1001/archinte.158.7.741>
- [16] Tonkin, A. and Wing, L. (1996) Management of Isolated Systolic Hypertension. *Drugs*, **51**, 738-749. <https://doi.org/10.2165/00003495-199651050-00003>
- [17] Messerli, F.H., Williams, B. and Ritz, E. (2007) Essential Hypertension. *The Lancet*, **370**, 591-603. [https://doi.org/10.1016/s0140-6736\(07\)61299-9](https://doi.org/10.1016/s0140-6736(07)61299-9)
- [18] Staessen, J.A., Wang, J., Bianchi, G. and Birkenhäger, W.H. (2003) Essential Hypertension. *The Lancet*, **361**, 1629-1641. [https://doi.org/10.1016/s0140-6736\(03\)13302-8](https://doi.org/10.1016/s0140-6736(03)13302-8)
- [19] Carey, R.M. (2008) Pathophysiology of Primary Hypertension. In: Tuma, R.F., Durán, W.N. and Ley, K., Eds., *Microcirculation*, Academic Press, 794-895.  
<https://doi.org/10.1016/b978-0-12-374530-9.00020-6>
- [20] Siddiqui, M.A., Mittal, P.K., Little, B.P., Miller, F.H., Akduman, E.I., Ali, K., *et al* (2019) Secondary Hypertension and Complications: Diagnosis and Role of Imaging. *RadioGraphics*, **39**, 1036-1055. <https://doi.org/10.1148/rg.2019180184>
- [21] Ott, C. and Schmieder, R.E. (2022) Diagnosis and Treatment of Arterial Hypertension 2021. *Kidney International*, **101**, 36-46.  
<https://doi.org/10.1016/j.kint.2021.09.026>
- [22] Hegde, S., Ahmed, I. and Aeddula, N. (2023) Secondary Hypertension. *StatPearls*.
- [23] Onusko, E. (2003) Diagnosing Secondary Hypertension. *American Family Physician*, **67**, 67-74.
- [24] Pullalarevu, R., Akbar, G. and Teehan, G. (2014) Secondary Hypertension, Issues in Diagnosis and Treatment. *Primary Care: Clinics in Office Practice*, **41**, 749-764.  
<https://doi.org/10.1016/j.pop.2014.08.001>
- [25] Rubin, S., Cremer, A., Boulestreau, R., Rigotherier, C., Kuntz, S. and Gosse, P. (2019) Malignant Hypertension: Diagnosis, Treatment and Prognosis with Experience from the Bordeaux Cohort. *Journal of Hypertension*, **37**, 316-324.  
<https://doi.org/10.1097/hjh.0000000000001913>
- [26] Sesoko, S. (1987) Predisposing Factors for the Development of Malignant Essential Hypertension. *Archives of Internal Medicine*, **147**, 1721-1724.  
<https://doi.org/10.1001/archinte.1987.00370100035007>
- [27] Kincaid-Smith, P. (1991) Malignant Hypertension. *Journal of Hypertension*, **9**, 893-900. <https://doi.org/10.1097/00004872-199110000-00002>
- [28] Mancia, G. and Giannattasio, C. (2015) Diagnostic and Therapeutic Problems of Isolated Systolic Hypertension. *Journal of Hypertension*, **33**, 33-43.  
<https://doi.org/10.1097/hjh.0000000000000424>
- [29] Hozawa, A., Ohkubo, T., Nagai, K., Kikuya, M., Matsubara, M., Tsuji, I., *et al* (2000) Prognosis of Isolated Systolic and Isolated Diastolic Hypertension as Assessed by Self-Measurement of Blood Pressure at Home: The Ohasama Study. *Archives of Internal Medicine*, **160**, 3301-3306. <https://doi.org/10.1001/archinte.160.21.3301>
- [30] Staessen, J.A., Gasowski, J., Wang, J.G., Thijs, L., Hond, E.D., Boissel, J., *et al* (2000) Risks of Untreated and Treated Isolated Systolic Hypertension in the Elderly: Meta-Analysis of Outcome Trials. *The Lancet*, **355**, 865-872.  
[https://doi.org/10.1016/s0140-6736\(99\)07330-4](https://doi.org/10.1016/s0140-6736(99)07330-4)
- [31] Kostis, J.B. (1997) Prevention of Heart Failure by Antihypertensive Drug Treatment in Older Persons with Isolated Systolic Hypertension. *JAMA: The Journal of the American Medical Association*, **278**, 212-216.  
<https://doi.org/10.1001/jama.1997.03550030052033>

- [32] Franklin, S.S., Thijs, L., Hansen, T.W., O'Brien, E. and Staessen, J.A. (2013) White-coat Hypertension: New Insights from Recent Studies. *Hypertension*, **62**, 982-987. <https://doi.org/10.1161/hypertensionaha.113.01275>
- [33] Huang, Y., Huang, W., Mai, W., Cai, X., An, D., Liu, Z., *et al.* (2017) White-Coat Hypertension Is a Risk Factor for Cardiovascular Diseases and Total Mortality. *Journal of Hypertension*, **35**, 677-688. <https://doi.org/10.1097/hjh.0000000000001226>
- [34] Celis, H. and Fagard, R.H. (2004) White-Coat Hypertension: A Clinical Review. *European Journal of Internal Medicine*, **15**, 348-357. <https://doi.org/10.1016/j.ejim.2004.08.001>
- [35] Sarafidis, P.A. and Bakris, G.L. (2008) Resistant Hypertension: An Overview of Evaluation and Treatment. *Journal of the American College of Cardiology*, **52**, 1749-1757. <https://doi.org/10.1016/j.jacc.2008.08.036>
- [36] Vongpatanasin, W. (2014) Resistant Hypertension: A Review of Diagnosis and Management. *JAMA*, **311**, 2216-2224. <https://doi.org/10.1001/jama.2014.5180>
- [37] Myat, A., Redwood, S.R., Qureshi, A.C., Spertus, J.A. and Williams, B. (2012) Resistant Hypertension. *BMJ*, **345**, e7473. <https://doi.org/10.1136/bmj.e7473>
- [38] Giles, T.D., Berk, B.C., Black, H.R., Cohn, J.N., Kostis, J.B., Izzo, J.L., *et al.* (2005) Expanding the Definition and Classification of Hypertension. *The Journal of Clinical Hypertension*, **7**, 505-512. <https://doi.org/10.1111/j.1524-6175.2005.04769.x>
- [39] Bell, E.T. and Pedersen, A.H. (1930) The Causes of Hypertension. *Annals of Internal Medicine*, **4**, 227-237.
- [40] Muntner, P., Shimbo, D., Carey, R.M., Charleston, J.B., Gaillard, T., Misra, S., *et al.* (2019) Measurement of Blood Pressure in Humans: A Scientific Statement from the American Heart Association. *Hypertension*, **73**, e35-e66. <https://doi.org/10.1161/hyp.0000000000000087>
- [41] Hauspurg, A., Seely, E.W., Rich-Edwards, J., Hayduchok, C., Bryan, S., Roche, A.T., *et al.* (2023) Postpartum Home Blood Pressure Monitoring and Lifestyle Intervention in Overweight and Obese Individuals the First Year after Gestational Hypertension or Pre-Eclampsia: A Pilot Feasibility Trial. *BJOG: An International Journal of Obstetrics & Gynaecology*, **130**, 715-726. <https://doi.org/10.1111/1471-0528.17381>
- [42] Paiva, A.M.G., Gomes, M.I.C.M., Silva, É.A.A., Feitosa, A.D.M., Malachias, M.V.B., Sposito, A.C., *et al.* (2023) Should Arm Positioning Matter in the Diagnosis of Orthostatic Hypotension and Hypertension? *Journal of Hypertension*, **42**, 186-188. <https://doi.org/10.1097/hjh.0000000000003571>
- [43] Choi, J., Kang, Y., Park, J., Joung, Y. and Koo, C. (2023) Development of Real-Time Cuffless Blood Pressure Measurement Systems with ECG Electrodes and a Microphone Using Pulse Transit Time (PTT). *Sensors*, **23**, Article 1684. <https://doi.org/10.3390/s23031684>
- [44] Pickering, T.G. and Gerin, W. (1990) Cardiovascular Reactivity in the Laboratory and the Role of Behavioral Factors in Hypertension: A Critical Review. *Annals of Behavioral Medicine*, **12**, 3-16. [https://doi.org/10.1207/s15324796abm1201\\_1](https://doi.org/10.1207/s15324796abm1201_1)
- [45] Vakulenko, I.M., Ruznyaeva, D.S., Manukian, R.A., Makaeva, D.S.A., Ulisova, M.S., Mikheeva, A.A. and Gruzdova, O.G. (2024) An Integrated Approach to Managing Arterial Blood Pressure and Its Impact on Brain Health. *Revista Latinoamericana de Hipertension*, **19**, 233-238.
- [46] Steijlen, A.S., Jansen, K.M., Albayrak, A., Verschure, D.O. and Van Wijk, D.F. (2018) A Novel 12-Lead Electrocardiographic System for Home Use: Development and Usability Testing. *JMIR mHealth and uHealth*, **6**, e10126. <https://doi.org/10.2196/10126>

- [47] White-Al Habeeb, N.M.A., Higgins, V., Wolska, A., Delaney, S.R., Remaley, A.T. and Beriault, D.R. (2023) The Present and Future of Lipid Testing in Cardiovascular Risk Assessment. *Clinical Chemistry*, **69**, 456-469. <https://doi.org/10.1093/clinchem/hvad012>
- [48] Oparil, S. (2003) Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT): Practical Implications. *Hypertension*, **41**, 1006-1009. <https://doi.org/10.1161/01.hyp.0000070905.09395.f6>
- [49] Morledge, J.H., Ettinger, B., Aranda, J., McBarron, F., Barra, P., Gorwit, J., *et al.* (1986) Isolated Systolic Hypertension in the Elderly: A Placebo-Controlled, Dose-Response Evaluation of Chlorthalidone. *Journal of the American Geriatrics Society*, **34**, 199-206. <https://doi.org/10.1111/j.1532-5415.1986.tb04203.x>
- [50] Webster, I., Fowler, G., Jeffers, T., Lyons, D., Witte, K., Crichton, W., *et al.* (1993) A Comparison of Amlodipine with Enalapril in the Treatment of Isolated Systolic Hypertension. *British Journal of Clinical Pharmacology*, **35**, 499-505. <https://doi.org/10.1111/j.1365-2125.1993.tb04176.x>
- [51] Narvaez, E.D., D'Souza, K. and Rivera, V. (2019) Common Chronic Conditions. In: Chun, A., Ed., *Geriatric Practice*, Springer International Publishing, 139-155. [https://doi.org/10.1007/978-3-030-19625-7\\_11](https://doi.org/10.1007/978-3-030-19625-7_11)
- [52] Gangaram, R., Ojwang, P.J., Moodley, J. and Maharaj, D. (2005) The Accuracy of Urine Dipsticks as a Screening Test for Proteinuria in Hypertensive Disorders of Pregnancy. *Hypertension in Pregnancy*, **24**, 117-123. <https://doi.org/10.1081/prg-200059849>
- [53] Volpe, M. (2007) Microalbuminuria Screening in Patients with Hypertension: Recommendations for Clinical Practice. *International Journal of Clinical Practice*, **62**, 97-108. <https://doi.org/10.1111/j.1742-1241.2007.01620.x>
- [54] O'Rourke, M.F. and Hashimoto, J. (2007) Mechanical Factors in Arterial Aging. *Journal of the American College of Cardiology*, **50**, 1-13. <https://doi.org/10.1016/j.jacc.2006.12.050>
- [55] Kakaletsis, N., Protogerou, A.D., Kotsis, V., Vemmos, K., Korompoki, E., Kollias, A., *et al.* (2024) Advanced Vascular Aging and Outcomes after Acute Ischemic Stroke: A Systematic Review and Meta-Analysis. *Journal of Human Hypertension*, **38**, 676-686. <https://doi.org/10.1038/s41371-024-00961-y>
- [56] Davis, B.R., Langford, H.G., Blaurock, M.D., Curb, J.D., Polk, B.F. and Shulman, N.B. (1987) The Association of Postural Changes in Systolic Blood Pressure and Mortality in Persons with Hypertension: The Hypertension Detection and Follow-Up Program Experience. *Circulation*, **75**, 340-346. <https://doi.org/10.1161/01.cir.75.2.340>
- [57] Kario, K., Eguchi, K., Hoshida, S., Hoshida, Y., Umeda, Y., Mitsuhashi, T., *et al.* (2002) U-Curve Relationship between Orthostatic Blood Pressure Change and Silent Cerebrovascular Disease in Elderly Hypertensives: Orthostatic Hypertension as a New Cardiovascular Risk Factor. *Journal of the American College of Cardiology*, **40**, 133-141. [https://doi.org/10.1016/s0735-1097\(02\)01923-x](https://doi.org/10.1016/s0735-1097(02)01923-x)
- [58] Algharably, E.A., Meinert, F., Januszewicz, A. and Kreutz, R. (2024) Understanding the Impact of Alcohol on Blood Pressure and Hypertension: From Moderate to Excessive Drinking. *Kardiologia Polska*, **82**, 10-18. <https://doi.org/10.33963/v.kp.98704>
- [59] Wacika, D.N.G.S., Permatananda, P.A.N.K. and Suyasa, E.A. (2024) Relationship between Physical Activity and Hypertension in Adults in the Working Area of Puskesmas Tampaksiring I. *Qanun Medika-Medical Journal Faculty of Medicine Muhammadiyah Surabaya*, **8**, 79-86. <https://doi.org/10.30651/jqm.v8i01.18840>
- [60] Katsi, V., Manta, E., Fragoulis, C. and Tsioufis, K. (2024) Weight Loss Therapies and

- Hypertension Benefits. *Biomedicines*, **12**, Article 2293.  
<https://doi.org/10.3390/biomedicines12102293>
- [61] Kusko, D.A., Blake, J. and Williams, R. (2023) A Narrative Review of the Effects of Mindfulness on Sleep and Hypertension. *Current Hypertension Reports*, **26**, 91-97.  
<https://doi.org/10.1007/s11906-023-01279-9>
- [62] Tan, J.L. and Thakur, K. (2023) Systolic Hypertension. StatPearls Publishing.
- [63] Gasowski, J., Staessen, J., Celis, H., Fagard, R., Thijs, L., Birkenhäger, W., *et al.* (1999) Systolic Hypertension in Europe (Syst-Eur) Trial Phase 2: Objectives, Protocol, and Initial Progress. *Journal of Human Hypertension*, **13**, 135-145.  
<https://doi.org/10.1038/sj.jhh.1000769>
- [64] Morales-Olivas, F.J. (2024) Diuretics Use in the Management of Hypertension. *Hipertensión y Riesgo Vascular*, **41**, 186-193.  
<https://doi.org/10.1016/j.hipert.2024.03.004>
- [65] Wing, L.M., Russell, A.E., Tonkin, A.L., Bune, A.J., West, M.J. and Chalmers, J.P. (1994) Felodipine, Metoprolol and Their Combination Compared with Placebo in Isolated Systolic Hypertension in the Elderly. *Blood Pressure*, **3**, 82-89.  
<https://doi.org/10.3109/08037059409101526>
- [66] Giles, T.D. (1990) Treatment of Isolated Systolic Hypertension with Labetalol in the Elderly. *Archives of Internal Medicine*, **150**, 974-976.  
<https://doi.org/10.1001/archinte.1990.00390170036009>
- [67] Applegate, W.B. (1994) Impact of the Treatment of Isolated Systolic Hypertension on Behavioral Variables: Results from the Systolic Hypertension in the Elderly Program. *Archives of Internal Medicine*, **154**, 2154-2160.  
<https://doi.org/10.1001/archinte.1994.00420190047006>
- [68] Foody, J.M., Benner, J.S. and Frishman, W. (2007) Adherence. *The Journal of Clinical Hypertension*, **9**, 271-275. <https://doi.org/10.1111/j.1524-6175.2007.06475.x>