Published on 1st of every month
SUPPLEMENT TO JAPI | May 2026 | Volume 75 | Issue 5 | ISSN: 0004-5772

Journal of The Association of Physicians of India

JAPI

Editor-in-Chief: **Prof. Dr. Nandini Chatterjee**

Special Issue on

Indian Hypertension Guidelines-V

INDIAN HYPERTENSION GUIDELINES-V

2025-2026

Journal of THE ASSOCIATION OF PHYSICIANS OF INDIA

JAPI App: myJAPI | www.japi.org

JAPI JOURNAL OF THE ASSOCIATION OF PHYSICIANS OF INDIA
Editor-in-Chief: **Prof. Dr. Nandini Chatterjee**

Subscription Information
Journal of The Association of Physicians of India is published monthly. The annual subscription is ₹15,000 (India). The Journal is dispatched within India by surface mail.

Business Correspondence
Enquiries concerning subscription, advertisement, etc. should be addressed to **Prof. Dr. Nandini Chatterjee**, Editor-in-Chief, JAPI, Unit No. 3301, Prestige Turf Tower 'D', Shakti Mill Lane, Off. Dr. E. Moses Road, Near Mahalaxmi Station (West), Mumbai-400 011.
Mobile number: 7710020034/7710029211
***e-mail*: onlinejapi@gmail.com/ nandinichatterjee.japi@gmail.com/ api.hdo@gmail.com**

Published and Edited by
Prof. Dr. Nandini Chatterjee, on behalf of **The Association of Physicians of India**, Journal of The Association of Physicians of India, Unit No. 3301, Prestige Turf Tower 'D', Shakti Mill Lane, Off. Dr. E. Moses Road, Near Mahalaxmi Station (West), Mumbai-400 011.
Editor-in-Chief: **Prof. Dr. Nandini Chatterjee.**

***Advertorial Enquiry*:**
Prof. Dr. Nandini Chatterjee,
Editor-in-Chief, JAPI,
Unit No. 3301, Prestige Turf Tower 'D',
Shakti Mill Lane, Off. Dr. E. Moses Road,
Near Mahalaxmi Station (West),
Mumbai-400 011.
Mobile number: 7710020034/7710029211
***e-mail*: onlinejapi@gmail.com/ nandinichatterjee.japi@gmail.com**

Jaypee Brothers Medical Publishers (P) Ltd.
New Delhi

JAPI App: myJAPI
www.japi.org

Association of Physicians of India

GOVERNING BODY (2026–2027)

President-Elect
Ashok K Taneja (Gurugram) (2027)

President
G Narsimulu (Hyderabad) (2027)

Past President
Jyotirmoy Pal (Barrackpur) (2027)

Vice Presidents
MPS Chawla (New Delhi) (2027)
Sekhar Chakraborty (Siliguri) (2027)
Ravikeerthy M (Bengaluru) (2029)

Hon. General Secretary
Puneet Saxena (Jaipur) (2027)

Jt. Secretary (HQ)
Rakesh Bhadade (Mumbai) (2028)

Hon. Treasurer
Amit Saraf (Mumbai) (2029)

Members

Nihar Mehta (Mumbai)	(2027)	**Soumitra Ghosh** (Kolkata)	(2028)	**Mahesh Kumar Dave** (Udaipur)	(2029)
Aditya Prakash Misra (New Delhi)	(2027)	**Pradeep Bhaumik** (Agartala)	(2028)	**Udas C Ghosh** (Kolkata)	(2029)
Nandini Chatterjee (Kolkata)	(2027)	**Sangram S Biradar** (Gulbarga)	(2028)	**L Muthumani** (Trichy)	(2029)
Gautam Bhandari (Jodhpur)	(2027)	**Anupam Prakash** (New Delhi)	(2028)	**Jayanta Kumar Panda** (Cuttack)	(2029)
AK Gupta (Agra)	(2027)	**M Pavan Kumar** (Warangal)	(2028)	**R Chandani** (Kozhikode)	(2029)
L Srinivasa Murthy (Bengaluru)	(2027)	**Pramod Kumar Sinha** (Gaya)	(2028)	**Braj Kishore Singh** (Aurangabad)	(2029)

Zonal Members

North Zone	**AK Singh** (Varanasi)	(2029)	Mid South Zone	**KR Jawaharlal** (Kakinada)	(2029)
North West Zone	**Ajay Mahajan** (Hisar)	(2029)	South Zone	**S Chandrasekhar** (Chennai)	(2029)
Central Zone	**GD Ramchandani** (Kota)	(2029)	Mid East Zone	**Amit Kumar Das** (Muzaffarpur)	(2029)
West Zone	**Anil Kumar Kulshrestha** (Ahmedabad)	(2029)	East Zone	**Debasis Chakrabarti** (Siliguri)	(2029)
North East Zone	**Dwijen Das** (Silchar)	(2029)			

Invited Members

Editor-in-Chief, API Textbook
KK Pareek (Kota)

Chairman, Finance Committee
Amal Kumar Banerjee (Kolkata)

Editor-in-Chief, JAPI
Nandini Chatterjee (Kolkata)

Chairman API Credential Committee
YSN Raju (Hyderabad)

Chairman, API House Committee
Anil Kumar Kulshrestha (Ahmedabad)

Ex-Officio Members

Dean, ICP
Girish Mathur (Kota)

Director, PRF
A Muruganathan (Tirupur)

Co-opted Members

Jt. Secretary (President's Place)
G Vishesh (Hyderabad)

Armed Forces Medical Services
Vivek Hande (Delhi)

Organizing Secretary, APICON 2026 (Patna)
Kamlesh Tewary (Muzaffarpur)

Organizing Secretary, APICON 2027 (Gurgaon)
Munish Prabhakar (Gurgaon)

Indian College of Physicians

FACULTY COUNCIL (2026–2027)

Chairman
G Narsimulu (Hyderabad) (2027)

Dean
Girish Mathur (Kota) (2027)

Dean-Elect
S Arulrhaj (Tuticorin) (2027)

Vice Deans
K Mugundhan (Chennai) (2027)
V Palaniappen (Dindigul, TN) (2028)
Prakesh Keshwani (Jaipur) (2029)

Hon. Gen. Secretary
Puneet Saxena (Jaipur) (2027)

Past Dean
Kamlesh Tewary (Muzaffarpur) (2027)

Jt. Secretary (HQ)
Rakesh Bhadade (Mumbai) (2028)

Jt. Secretary (Dean's Place)
Ashutosh Chaturvedi (Jaipur) (2027)

Hon. Treasurer
Amit Saraf (Mumbai) (2029)

Elected Members

Munish Prabhakar (Gurugram)	(2027)	**Hem Shankar Sharma** (Bhagalpur)	(2028)	**Prasanta Dhingia** (Dibugarh)	(2029)
S Sreenivasa Kamath (Kochi)	(2027)	**Ashis Kumar Saha** (Kolkata)	(2028)	**Rabindra Kumar Modi** (Purnia)	(2029)
E Prabhu (Chennai)	(2027)	**Suresh V Sagarad** (Raichur)	(2028)	**Anil Gomber** (New Delhi)	(2029)
Mahesh Marda (Hyderabad)	(2027)	**Partha Sarkar** (Kolkata)	(2029)	**Vikram Londhey** (Mumbai)	(2029)
Sandeep Garg (New Delhi)	(2028)	**Naval Chandra** (Hyderabad)	(2029)		

Ex-Officio Members

President-Elect
Ashok Taneja (Gurgaon)

Editor-in-Chief, JAPI
Nandini Chatterjee (Kolkata)

Director, PRF
A Muruganathan (Tirupur)

Editor-in-Chief, API Textbook
KK Pareek (Kota)

Invited Member
Chairman, Credentials Committee
Shyam Sundar (Varanasi)

Physicians Research Foundation

BOARD OF DIRECTORS (2026–2027)

Chairman
G Narsimulu (Hyderabad) (2027)

Director
A Muruganathan (Tirupur) (2027)

Director Elect
Sanjeev Maheshwari (Ajmer) (2027)

Hon. General Secretary
Puneet Saxena (Jaipur) (2027)

Jt. Secretary (Director's Place)
R Rajasekaran (Kumbakonam) (2027)

Hon. Treasurer
Amit Saraf (Mumbai) (2029)

Members

Devendra Prasad Singh (Bhagalpur)	(2027)	**Ghanshyam Pangtey** (New Delhi)	(2028)	**Ramesh Aggarwal** (New Delhi)	(2029)
Puneet Rijhwani (Jaipur)	(2027)	**SS Dariya** (Jaipur)	(2029)	**Prabhat Pandey** (Durg)	(2029)
Sudhir Mehta (Jaipur)	(2028)				

Invited Members

Editor-in-Chief, JAPI
Nandini Chatterjee (Kolkata)

Dean, ICP
Girish Mathur (Kota)

Editor-in-Chief, API Textbook
KK Pareek (Kota)

JAPI
JOURNAL OF THE ASSOCIATION OF PHYSICIANS OF INDIA
Editor-in-Chief: **Prof. Dr. Nandini Chatterjee**

Supplement Copy – Online Only

Indian Hypertension Guideline V. 2025–2026

Contents

List of Members – I.G.H. V (2025–2026)

Steering Committee

Dr Nihar Mehta
Dr Girish Mathur
Dr Jyotirmoy Pal
Dr Ashok Taneja
Dr GS Wander
Dr C Venkatram
Dr KK Pareek
Dr GN Narsimulu
Dr Puneet Saxena
Dr A Muruganathan
Dr Nandini Chattetjee
Dr Milind Nadkar
Dr Amit saraf
Dr Mangesh Tiwaskar
Dr Agam Vora
Dr MK Das
Dr RK Singhal
Dr Shashank Joshi
Dr Jayant Panda
Dr Sekhar Chakrabarty
Dr HS Pathak
Dr Ravikeerthy

Executive Committee

Dr AK Banerjee
Dr Samar Banerjee
Dr Shyam B Bansal
Dr Pritam Barthakur
Dr BR Bansode
Dr Atul Bhasin
Dr Anil Bhansali
Dr Rakesh Bhadade
Dr Pradip Bhowmik
Dr Sangram Biradar
Dr Ashutosh Chaturvedi
Dr R Chandni
Dr Anand Chellappan
Dr M Chenniappan
Dr Amit Das
Dr Dijen Das
Dr Udas Ghosh
Dr Naresh Goyal
Dr Gagan Gunjan
Dr Rajeeb Gupta
Dr Uday Jadhav
Dr DG Jain
Dr HS Kohli
Dr Sanjay Kalra
Dr Satish Khadilkar
Dr Umesh Khanna
Dr Ashok Kripalani
Dr Bidita Khadelwal
Dr Jayesh Lele
Dr Anuj Maheshwari
Dr Ketan Mehta
Dr U Meenakshisundaram
Dr Ajit Mullaseri
Dr L Sreenivasa Murthy
Dr Tiny Nair
Dr SN Narasingan
Dr R Lakshmi Narasimhan
Dr Munish Prabhakar
Dr Kaushik Pandit
Dr CK Ponde
Dr Pravat Pandey
Dr Rishikesh Pai
Dr Namarta Rao
Dr Banshi Saboo
Dr Santosh Salagare
Dr Suresh Sagarod
Dr Manisha Sahay
Dr RK Sahay
Dr KK Sawalni
Dr Puneet Saxena
Dr Sunil Sathe
Dr Sengottuvelu
Dr OP Sharma
Dr SK Sharma
Dr DP Singh
Dr Nirmal Surya
Dr Rajesh Swarnakar
Dr Sunita Tandulwadkar
Dr Kamlesh Tiwari
Dr Vijay Viswanathan

List of Members

I.G.H. IV (2019)

Core Committee

Convenor

Dr Siddharth N Shah, Mumbai

Members

Dr Aspi R Billimoria, Mumbai
Dr Sandhya A Kamath, Mumbai
Dr M Maiya, Bangalore
Dr Sukumar Mukherjee, Kolkata
Dr YP Munjal, New Delhi
Dr GS Wander, Ludhiana
Dr Nihar Mehta, Mumbai

I.G.H. III (2013)

Core Committee

Convenor

Dr Siddharth N Shah, Mumbai

Members

Dr Aspi R Billimoria, Mumbai
Dr Sandhya A Kamath, Mumbai
Dr M Maiya, Bangalore
Dr Sukumar Mukherjee, Kolkata
Dr YP Munjal, New Delhi
Dr GS Wander, Ludhiana
Dr Nihar Mehta, Mumbai

I.G.H. II (2007)

Core Committee

Convenor

Dr Siddharth N Shah, Mumbai

Members

Dr M Paul Anand, Mumbai
Dr Sandhya A Kamath, Mumbai
Dr M Maiya, Bangalore
Dr Sukumar Mukherjee, Kolkata
Dr YP Munjal, New Delhi
Dr GS Wander, Ludhiana

I.G.M.H. I (2001)

Core Committee

Convenor

Dr Siddharth N Shah, Mumbai

Members

Dr M Paul Anand
Dr YP Munjal
Dr BM Hegde
Dr Sukumar Mukherjee
Dr GS Wander

Preamble

Hypertension significantly contributes to cardiovascular morbidity and mortality on a global scale, including in India. In light of our particular geographical and climatic conditions, ethnic backgrounds, dietary practices, literacy levels, and socio-economic factors, there are important differences in the manifestation and management of this disease in our country that warrant our attention. Therefore, the Association of Physicians of India (API), the Cardiological Society of India (CSI), the Indian College of Physicians (ICP), and the Hypertension Society of India (HSI) have created the "FIRST INDIAN GUIDELINES FOR THE MANAGEMENT OF HYPERTENSION—2001."

The second edition of the Indian guidelines was published in 2007, followed by the third edition, known as the Indian Guidelines on Hypertension (IGH-III), in 2013. The fourth edition was published in 2019. Over the past 6 years, since the last edition, there have been significant advancements in the management of hypertension. Significant updates include the ACC/AHA's revised definition of hypertension, which we have decided not to adopt, thereby continuing with the previous definition.

Additionally, there have been modifications in the target blood pressure goals, an increased emphasis on self-home blood pressure monitoring (SBPM) and ambulatory blood pressure monitoring (ABPM), renewed interest in renal denervation therapy due to recent data, and an increased use of spironolactone for resistant hypertension.

Beyond this, we have also included epidemiological data on hypertension and hypertension-mediated organ damage (HMOD). Significant revisions have been noted in the guidelines published in 2023 and 2024, making it necessary to review the literature from an Indian perspective and thus provide hypertension management guidelines for Indian physicians. These guidelines have been prepared as a reference for treating physicians. We have also included updated prevalence statistics based on the latest nationwide and regional data on hypertension across different age groups, genders, and socioeconomic segments, along with insights into India's burden of hypertension and cardiovascular disease.

The present state of practice patterns based on evidence-based medicine has been summarized. The purpose is not to comprehensively address the subject of hypertension but to deliver relevant information derived from literature, along with an evaluation of the latest guidelines from various national organizations, such as the ACC/AHA guidelines and the European ESC/ESH guidelines. The primary aim of these guidelines is to offer balanced information to guide clinicians, rather than rigid rules that would constrain their judgment about the management of individual adult patients with varying personal, medical, social, economic, ethnic, and clinical characteristics. These guidelines do not provide a framework for hypertension management in children and adolescents.

We acknowledge 6 Sigma Healthcare Communication for their contribution in medical writing, along with API members for their invaluable support and commitment to delivering high-quality, accurate content for the Indian Guideline on Hypertension–V.

Methodology

In accordance with the earlier guidelines, a Steering Committee was formulated, and the members were assigned various sections of the guidelines. Each steering committee member, along with members of the Executive Committee, worked on their allotted sections. The executive committee comprised physicians and specialists from various regions of the country, whose insights have been integrated into the content. Once the individual sections were formulated, a joint meeting was conducted, and the draft of the guidelines was completed. Additionally, the document was endorsed by various organizations across India, including the Hypertension Society of India, Indian Society of Nephrology, Indian Academy of Neurology, Endocrine Society of India, Association of Clinical Diabetology, and the Federation of Obstetric and Gynecological Societies of India.

We hope these guidelines will help practicing physicians to address this very important public health challenge. The treatment of essential hypertension is a life-long commitment and should not be stopped even when the blood pressure (BP) is stabilized without consulting one's physician. The core committee recognizes that the responsible physician's judgment and decisions remain paramount for individual adult patients.

Endorsements

- Hypertension Society of India (HSI)
- Indian Society of Nephrology (ISN)
- Indian Academy of Neurology (IAN)
- Endocrine Society of India (ESI)
- Association of Clinical Diabetology (ACD)
- The Federation of Obstetric and Gynaecological Societies of India (FOGSI)

What is New in Indian Guidelines on Hypertension–V

The latest issue of the "Indian Guidelines on Hypertension (IGH-V)," presents a comprehensive update for 2025. These revisions address critical gaps and advancements in hypertension management, reflecting the latest research and clinical practices specifically for the Indian population. An overview of the key updates is provided below:

Updated Prevalence Statistics

- Updated statistics from national and regional data sources are integrated in IGH V, offering detailed insights into state-wise hypertension prevalence across different age groups, genders, and socio-economic strata. The guidelines address the evolving burden of hypertension and its correlation with CVD.
- Awareness Gaps in Hypertension Detection and Control: IGH-V also addresses the gaps in awareness and control of hypertension in India. Despite progress, a significant portion of the population remains undiagnosed or inadequately treated, signifying the need for public health campaigns and improved access to care.

Cardiovascular Disease Risk-stratification Algorithm

A significant feature is the introduction of a newly developed cardiovascular disease risk-stratification algorithm. This tool guides clinicians in the personalization of blood pressure management strategies by categorizing patients into different CV risk profile groups. Factors such as age, comorbidities, high-risk clinical conditions, as well as certain investigations are incorporated into the algorithm, providing a structured approach to treatment.

Classifications and Categories of High Blood Pressure

Various categories of high blood pressure have been generated in order to simplify the clinical determination and management of hypertension.

Measurement of Blood Pressure

Methods of measurement of clinic BP, ambulatory BP, and self-monitoring of BP (Home BP) have been illustrated for ease of understanding.

Revised Management Algorithms

IGH-V refines management protocols by introducing:

- Revised blood pressure thresholds: The thresholds to initiate lifestyle management versus pharmacotherapy have been fine-tuned and made into simple tables and algorithms for quick reference and guidance.
- Revised blood pressure targets: Customized targets have been set for specific populations, including high-risk groups such as individuals with diabetes, kidney disease, or existing CVD.
- Step-by-step therapy pathways: Algorithms have been developed to guide physicians through the step-by-step management of hypertensive patients, including recommendations for drug selection and treatment escalation.
- Management of resistant hypertension: Specific recommendations for managing patients who fail to respond to conventional therapies, incorporating pharmacological options as well as interventional therapies that are available in our country.

Updated Drug Recommendations

The guidelines align drug choices with the latest evidence:

- First-line and add-on therapies: Recommendations for effective drug combinations are provided.
- Combination therapies: The guidelines highlight the benefits of fixed-dose combinations in improving treatment efficacy and patient adherence. The importance of single-pill combination therapy for better blood pressure control and simplified treatment regimens has also been emphasized.
- Beta-blockers: A significant update on the inclusion and role of beta-blockers in managing hypertension in the Indian context has been presented.

Special Populations

IGH-V expands guidance for managing hypertension in special groups, such as elderly patients, pregnant women, patients with cancer, and postoperative hypertension in addition to various comorbidities such as diabetes, kidney disease, COPD, cardiovascular and cerebrovascular disease.

Technology in Hypertension

The role of technology in hypertension management has been highlighted, including the use of telemedicine, virtual clinics, mobile apps, and social media platforms.

1. Updated prevalence data: State-wise statistics across age, gender, and socioeconomic groups, highlighting the growing hypertension-CVD burden in India.
2. Awareness gaps: Significant portions of Indians remain undiagnosed or undertreated, calling for stronger public health outreach.
3. New CV risk-stratification algorithm: Personalizes BP management by categorizing patients based on age, comorbidities, and investigations.
4. Simplified BP classifications: Clearer categories to ease clinical diagnosis and management decisions.
5. Standardized BP measurement: Guidance on clinic BP, ambulatory monitoring, and home BP self-monitoring.
6. Revised thresholds and targets: Updated cut-offs for when to start lifestyle changes vs. drugs, with customized targets for high-risk groups (diabetes, CKD, CVD).
7. Step-by-step therapy pathways: Structured algorithms for drug selection and treatment escalation.
8. Resistant hypertension management: Specific protocols including pharmacological and interventional options available in India.
9. Updated drug recommendations: Emphasis on fixed-dose combinations and single-pill combinations for better adherence and control; updated role of beta-blockers.
10. Special populations & technology: Expanded guidance for elderly, pregnant women, cancer patients, and various comorbidities, plus integration of telemedicine, apps, and virtual clinics.

Definition and Classification

Definition of Hypertension

Hypertension is defined as the sustained elevation of systemic arterial pressure above a certain threshold value or any level of blood pressure in a patient taking antihypertensive medications. For chronic uncontrolled hypertension, every 20 mm Hg increase in systolic blood pressure (SBP), or 10 mm Hg increase in diastolic blood pressure (DBP), is associated with a doubling of vascular mortality. Risk of CV death increases two-fold if BP rises to 135/85 mm Hg, four-fold if BP rises to 155/95 mm Hg, and eightfold at 175/105 mm Hg.[1–3] All definitions of hypertension issued by various international bodies are arbitrary. There is some evidence that the risk of cardiovascular events in Asian Indians is higher at relatively lower levels of BP. Recently, the ACC/AHA guidelines have changed the definition of hypertension to 130/80.[4] However, the European guidelines and frameworks from other countries still maintain the earlier threshold of hypertension at 140/90 mm Hg.[5] The IGH-V will continue with the previous definition of 140/90 mm Hg.[6]

Hypertension in adults aged 18 years and older is defined as systolic blood pressure (SBP) of 140 mm Hg or greater and/or diastolic blood pressure (DBP) of 90 mm Hg or greater, or any level of blood pressure in patients taking antihypertensive medication.

Hypertension-mediated end-organ damage may lead to the impairment of the heart, kidneys, brain, vasculature, and other organs. Therefore, the therapeutic goal is to maintain the BP in the normal range and to reduce the overall health risks to the patients.[7]

Need for the Hypertension Classification

- To determine the severity of the elevated blood pressure.
- To understand the basic pathophysiology.
- To determine when drug therapy should be initiated and adjusted.
- To prognosticate.
- To predict present and future complications.
- To plan the appropriate management.

Classification

Although the classification of adult blood pressure is somewhat arbitrary, it is useful for clinicians who make treatment decisions based on a constellation of factors along with the actual level of blood pressure. Table 1 provides a classification of blood pressure for adults (aged 18 years and older).[8,9]

This classification is applicable to individuals who are not taking antihypertensive medication and who do not have an acute illness, and is based on the average of two or more blood pressure readings taken at least on two occasions, one to three weeks apart, after the initial screening. In addition to classifying stages of hypertension on the basis of average blood pressure levels, clinicians should consider the presence or absence of target organ disease and additional risk factors.

The positive linear relationships between SBP, DBP, and cardiovascular risk have long been recognized. This relationship is strong, continuous, graded, consistent, independent, predictive, and etiologically significant for those with and without coronary heart disease.[10,11] For persons over the age of 60 years, SBP is more important than DBP as a CVD risk factor.[12] SBP is more difficult to control than DBP,[13,14] but needs to be controlled as aggressively as DBP. When SBP and DBP fall into different categories, the higher category should be selected to classify the individual's blood pressure. The definition and classification of hypertension is based on office readings by the physicians. The HBPM may be taken into account for staging and therapy of the patient. More recently, the SPRINT study used automatic office blood pressure (AOBP) recordings which are not always feasible and are thus not recommended for routine use. AOBP readings are 10–15/5–7 mm Hg lower than the office BP readings, which we routinely use for the definition of hypertension.[15]

The classification of hypertension should still largely be based on office recordings by the physician (Table 1).

Table 2 shows Ambulatory blood pressure monitoring (ABPM) based classification for normal and hypertensive values across 24-hour, daytime, and nighttime BP measurements.

The cut-off levels for defining hypertension for the Office BP, HBPM, and ABPM are given in Table 3.

Additional Classifications and Categories of Hypertension[6]

For additional classifications and categories of hypertension, see Table 4 for further details.

Table 1: Classification of blood pressure for adults aged 18 years and older

Category	*Systolic (mm Hg)*		*Diastolic (mm Hg)*
Optimal/ideal BP	<120	and	<80
Normal BP	<130	and	<85
High-normal BP	130–140	or	85–89
Hypertension			
Mild	140–160	or	90–100
Moderate	160–180	or	100–110
Severe	≥180	or	≥110
Isolated Systolic Hypertension	≥140	and	<90
Isolated Diastolic Hypertension	<140	and	≥90

Table 2: Ambulatory blood pressure measurement

Category	*Normal (mm Hg)*	*Hypertension (mm Hg)*
24-hour average	<130/80	≥130/80
Daytime/awake	<135/85	≥135/85
Asleep / Nighttime	<120/70	≥120/70

Table 3: Diagnosis of hypertension

	SBP (mm Hg)	*DBP (mm Hg)*
Office BP	≥140	≥90
Self-monitored/home BP (mean)	≥135	≥85
Ambulatory BP 24-hour (mean)	≥130	≥80
Ambulatory BP day-time (mean)	≥135	≥85
Ambulatory BP nighttime (mean)	≥120	≥70

Table 4: Classification of blood pressure based on various factors

A. Based on Types of BP (systolic, systolic and diastolic, isolated diastolic)		
Isolated systolic hypertension (ISH)	*Isolated diastolic hypertension (IDH)*	*High pulse pressure (HPP) hypertension*
Systolic BP >140 mm Hg and the diastolic BP <90	Systolic BP <140 mm Hg and the diastolic BP ≥ 90 mm Hg	Normal pulse pressure is 30–50 mm Hg High systolic and low diastolic BP is a dangerous combination Physicians should rule out conditions such as aortic regurgitation, anemia, Beri Beri and hypothyroidism before making the diagnosis of HPP hypertension
Mild ISH: Systolic BP 140–159 mm Hg Moderate ISH: Systolic BP 160–179 mm Hg Severe ISH: Systolic BP ≥ 180 mm Hg	Isolated diastolic hypertension (IDH) No-grading	High pulse pressure hypertension (HPPH) No-grading
Develops due to the increased cardiac output in young patients and the increased aortic stiffness in the elderly patients	IDH may progress in the future to systolic and diastolic hypertension, Emerging evidence suggests it might confer a higher cardiovascular risk, especially in young patients. Outcomes are independent of baseline systolic BP More common in the younger individual of age less than 50 years IDH in those above 65 years should lead to a suspicion of secondary hypertension.	Any hypertension which has the pulse pressure of more than 50 mm Hg (high systolic BP >140 mm Hg and low diastolic BP < 70 mm Hg). Every 10 mm Hg increase in the pulse pressure increases the risk of coronary artery disease by 23% Pulse pressure of more than 50 mm Hg increases the risk of CVD, arrhythmias, stroke, etc.
B. Based on etiology (primary or secondary)		
Factors	*Primary hypertension*	*Secondary hypertension*
Control	Controllable	Difficult to control Suddenly becomes out of control
Cure	Not curable	Mostly curable
Onset	Middle age (30–50 years)	Abrupt onset Before 30 years of age IDH mainly develops after 65 years
BP pattern	Systolic and Diastolic and IDH	Hypertensive crisis
Confirmation of diagnosis	Rule out secondary hypertension	Appropriate investigations
Causes	Not identifiable	Refer to secondary hypertension section
C. Based on location [clinic (office-based) or self-monitored (home or workplace)]		
Self-monitored BP ≥ 135/85 mm Hg and ambulatory BP ≥ 130/80 mm Hg recorded over 24-hour period. Average daytime is ≥ 135/85 mm Hg; Average nighttime BP is ≥ 120/70 mm Hg. The term home BP may be replaced by the self-monitored BP or out of clinic BP as this BP monitoring may not essentially be in home, but may be at other places such as the workplace		
Hypertension in clinic and Normal BP in home: "White coat hypertension" with Clinic BP more than 140/90 mm Hg and out of clinic BP / self-monitored BP < 135/85 mm Hg		
Hypertension out of clinic and normal BP in clinic: "Masked hypertension" with Clinic BP < 140/90 mm Hg and out of clinic / self-monitored BP ≥ 135/85 mm Hg		
D. Based on time (day/night/24-hour)		
Isolated day time hypertension	*Isolated nocturnal hypertension*	
Clinic, out of clinic or self-monitored BP and ambulatory BP level compatible with a diagnosis of hypertension at the various times of day (see above)	Characterized by the nocturnal BP >120/70 mm Hg with daytime BP <135/85 mm Hg	
Prevalence is up to 90%	Prevalence is 6–10%	
–	Likely to occur in elderly, males, obese, those with a higher pulse rate at night and those with glycemic and lipid abnormalities	
–	Types Non-dipper: Night-time BP drops less than 10% of daytime levels Reverse-dipper: No drop or Increase in BP at nighttime Extreme dipper: Night-time BP drops to more than 20% of daytime levels	
Night-time BP measured from bedtime to rising (at least ≥6 readings/night over 2 days).		

Contd…

Contd…

E. Based on position (Supine/Standing)	
Standing hypertension	*Supine hypertension–Orthostatic hypotension (SH-OH)*
Postural Hypertension	SH-OH syndrome
Increase in systolic BP ≥ 20 mm Hg when assuming an upright position (head tilt to 70 degrees within the study) from supine position or a ≥ 20 mm Hg increase in SBP after standing	Autonomic dysfunction is characterized by hypertension in the supine position (BP ≥ 140/90 mm Hg) and hypotension (BP < 120/80 mm Hg) while assuming an upright position

F. Based on Complication (complicated and uncomplicated)		
Uncomplicated hypertension	*Complicated hypertension*	*Chronic hypertension*
No other associated risk factors	Associated with risk factors (smoking, dyslipidemia, diabetes, age above 60 years, post menopause, history of CAD, obstructive sleep apnea etc.)	Causes endothelial dysfunction in the small arteries of the kidneys, leading to impairment of normal arterial autoregulation. Can cause acute end-organ dysfunction and can manifest clinically as a hypertensive emergency. 1% to 2% of individuals living with chronic hypertension experience an episode of hypertensive emergency in their lifetime.[6] Chronic hypertension mediated repeated contraction against increased afterload results in left ventricular hypertrophy and eventually impaired diastolic filling as the hypertrophied ventricle fails to fully relax. Chronic hypertension leads to cellular remodeling that narrows the lumen of small vessels and causes atherosclerosis in large vessels, resulting in the increase the risk of myocardial infarction, stroke, and kidney failure.[7, 8]
(No HMOD or co-morbid conditions	With HMOD Brain: Cerebrovascular accident (CVA); infarct, hemorrhage, Transient ischemic attack Eye: Hypertensive retinopathy Heart: Arrhythmias, Angina, Left ventricular hypertrophy, Heart failure, Atrial fibrillation, Myocardial infarction Kidney: Albuminuria, Nephropathy, Renal failure. Vascular complications: including micro and macrovascular complications Or Comorbid conditions including Sleep apnea, bronchial asthma, chronic kidney disease, cancer, depression, extra drugs, frailty, goiter, high BMI, diabetes, etc.	

G. Based on presentation (acute)	
Acute severe hypertension: emergency	*Acute severe hypertension: non-emergency*
Acute sudden increase in BP ≥ 180/120 mm Hg	Acute sudden increase in BP ≥ 180/120 mm Hg
Associated with life-threatening organ damage	Without life-threatening organ damage
The BP of 160/100 mm Hg is considered acute severe hypertension in the setting of gestational hypertension and preeclampsia.	

H. Classification of Hypertension in Pregnancy
Chronic hypertension complicating pregnancy: Known case of hypertension or a case of hypertension detected before 20 weeks of gestation in the absence of neoplastic trophoblastic disease and multiple pregnancies.
Gestational hypertension: BP ≥140/90 mm Hg, detected beyond 20 weeks of gestation, returning to normal within the 42nd postpartum day; not associated with any other features of preeclampsia.
Preeclampsia: Gestational hypertension with new onset proteinuria and/or one or more adverse conditions or severe complications

Epidemiology of Hypertension

Global

Hypertension is a significant global health issue. It is a major risk factor for cardiovascular diseases (CVDs), including heart attacks and strokes, which are the leading causes of morbidity and mortality worldwide. Hypertension not only increases the likelihood of premature death but also contributes substantially to disability-adjusted life years (DALYs) and reduced quality of life.[16]

Cardiovascular diseases (CVDs) are the leading cause of death globally, taking an estimated 17.9 million lives each year.[16] CVDs are a group of disorders of the heart and blood vessels and include coronary heart disease, cerebrovascular disease, rheumatic heart disease and other conditions. More than four out of five CVD deaths are caused by heart attacks and strokes, and one third of these deaths occur prematurely in people under 70 years of age.[16]

According to the World Health Organization (WHO), an estimated 1.28 billion adults aged 30–79 years worldwide have hypertension. This number continues to grow, with projections indicating that by 2030, more than 1.5 billion individuals will be affected by the condition.[16] Notably, two-thirds of them live in low- and middle-income countries. where healthcare infrastructure and public health strategies to manage and control hypertension are often inadequate.[17]

High systolic BP remains the leading modifiable risk factor globally for attributable premature cardiovascular deaths, accounting for 10.8 million (95% CI: 9.15–12.1 million) cardiovascular deaths and 11.3 million (95% CI: 9.59–12.7 million) deaths overall. In particular, high systolic BP has been linked to ischemic heart disease and stroke-related deaths. Hypertension is responsible for 45% of deaths from heart disease and 35% from stroke.[18,19] The Global Burden of Disease 2019 (GBD 2019) estimates that 19% of global deaths are attributed to elevated BP.[19]

Uncontrolled hypertension can lead to severe complications, including heart disease, stroke, kidney failure, and vision loss (Tables 5 and 6).

The global distribution of hypertension is uneven, and its prevalence is heavily influenced by socio-economic factors, lifestyle choices, and regional health policies. While the prevalence in high-income countries (HICs) has stabilized or declined over the past few decades, low- and middle-income regions, particularly in Africa and South Asia, have seen an alarming rise in hypertension rates (Table 7).[19]

Hypertension in Low- and Middle-Income Countries (LMICs)

The situation in LMICs is particularly dire. As economic development and urbanization continue to spread across these regions, dietary patterns have changed, and sedentary lifestyles have become more common. These shifts contribute to the rising prevalence of hypertension and its related complications, including heart disease and stroke. In South Asia, for instance, a significant rise in premature cardiovascular events has been recorded, with individuals experiencing heart attacks approximately 10 years earlier than those in high-income countries.[19]

National

Reports on the prevalence of hypertension in India in the late nineties and early twentieth

Table 5: Percentage of hypertension-related deaths by complication[18]

Complication	*Percentage of hypertension-related deaths*
Heart disease	45%
Stroke	35%
Kidney disease	10%
Other complications	10%

Table 7: Hypertension prevalence by region

Region	*Prevalence (%)*
Africa	27.0
Americas	26.0
South-East Asia	24.0
Europe	23.0
Western Pacific	22.0
Eastern Mediterranean	21.0

Table 6: Global ranking of cardiovascular deaths by cause[19]

Rank	*Cause of death*	*Number of deaths*	*Deaths in 2021 (95% UI)*	*Number of DALYs (95% UI)*
1	Ischemic heart disease	9,440,000	(8,820,000–9,960,000)	185,000,000 (175,000,000–196,000,000)
2	Ischemic stroke	3,870,000	(3,550,000–4,170,000)	70,200,000 (64,500,000–76,800,000)
3	Intracerebral hemorrhage	3,460,000	(3,210,000–3,750,000)	78,600,000 (73,300,000–84,600,000)
4	Hypertensive heart disease	1,410,000	(1,170,000–1,560,000)	24,900,000 (20,900,000–27,200,000)
5	Rheumatic heart disease	391,000	(340,000–454,000)	13,400,000 (11,600,000–15,400,000)
6	Atrial fibrillation and flutter	366,000	(313,000–396,000)	8,200,000 (6,830,000–9,940,000)
7	Subarachnoid hemorrhage	365,000	(329,000–411,000)	10,400,000 (9,370,000–11,800,000)
8	Other cardiomyopathies	320,000	(289,000–348,000)	8,450,000 (7,800,000–9,170,000)
9	Other cardiovascular diseases	232,000	(212,000–252,000)	10,100,000 (8,500,000–11,900,000)
10	Aortic aneurysm	160,000	(144,000–170,000)	3,040,000 (2,820,000–3,210,000)
11	Nonrheumatic calcific aortic valve disease	151,000	(127,000–164,000)	2,140,000 (1,950,000–2,370,000)
12	Endocarditis	81,100	(74,400–90,400)	2,040,000 (1,880,000–2,270,000)
13	Lower extremity peripheral arterial disease	71,200	(61,400–76,300)	1,520,000 (1,230,000–2,010,000)
14	Alcoholic cardiomyopathy	66,000	(55,600–74,200)	2,190,000 (1,850,000–2,460,000)
15	Non-rheumatic degenerative mitral valve disease	38,600	(33,900–43,100)	924,000 (827,000–1,070,000)
16	Myocarditis	33,600	(27,100–38,000)	962,000 (810,000–1,090,000)
17	Pulmonary arterial hypertension	23,300	(20,000–26,000)	640,000 (565,000–726,000)
18	Other non-rheumatic valve diseases	2,120	(1,580–2,690)	51,500 (37,100–66,200)

DALY, disability-adjusted life year; UI, uncertainty interval

Table 8: Prevalence of hypertension among men and women aged 15 and over, according to background characteristics, India, 2019–21

Background characteristics	*Men*		*Women*		*Overall*	
	Prevalence of hypertension (%)	*Weighted sample*	*Prevalence of hypertension (%)*	*Weighted sample*	*Prevalence of hypertension (%)*	*Weighted sample*
Total	24.1	7,85,611	21.2	9,22,630	22.6	17,08,241
Age of household member (years)						
15–29	8.3	2,63,624	4.8	3,25,911	6.4	5,89,534
30–44	21.6	2,12,674	15.4	2,55,549	18.2	4,68,223
45–59	34.2	1,69,044	34.1	1,99,619	34.2	3,68,663
60 and over	45.5	1,40,188	51.3	1,41,410	48.4	2,81,598
Place of residence						
Urban	26.7	2,52,345	23.4	2,89,463	25.0	5,41,808
Rural	22.9	5,33,266	20.2	6,33,168	21.4	11,66,433
Region of residence						
North	24.8	1,07,673	20.6	1,26,859	22.5	2,34,533
Central	22.6	1,90,448	19.3	2,24,242	20.8	4,14,690
East	20.7	1,66,058	18.6	2,05,101	19.5	3,71,160
Northeast	23.0	26,791	20.4	30,061	21.6	56,852
West	22.6	1,25,109	21.9	1,34,099	22.3	2,59,207
South	30.0	1,69,531	26.1	2,02,268	27.9	3,71,799
Religion of the household head						
Hindu	24.0	6,54,793	20.9	7,62,342	22.4	14,17,134
Muslim	21.6	88,190	20.9	1,10,402	21.2	1,98,592
Others	30.4	42,627	26.6	49,887	28.4	92,515
Caste/Tribe of the household head						
None of them	26.2	2,04,388	23.8	2,39,551	24.9	4,43,940
Scheduled Caste (SC)	22.9	1,70,280	19.4	2,01,453	21.0	3,71,732
Scheduled Tribe (ST)	22.3	75,903	19.6	86,936	20.9	1,62,838
Other Backward Classes (OBC)	23.9	3,35,040	21.0	3,94,691	22.3	7,29,731
Current marital status						
Married	29.3	5,43,247	20.9	6,48,239	24.7	11,91,486
Unmarried	12.6	2,42,282	21.9	2,74,250	17.6	5,16,532
Highest educational level attained						
Non-literate	29.3	1,27,157	30.9	3,09,481	30.4	4,36,638
Primary	28.7	1,13,329	26.3	1,26,143	27.4	2,39,472
Secondary	21.9	4,13,798	14.5	3,79,091	18.4	7,92,889
Higher	22.0	1,30,726	10.9	1,07,557	17.0	2,38,283
Wealth index						
Poorest	19.6	1,40,038	18.5	1,74,228	19.0	3,14,266
Poorer	20.9	1,53,985	19.1	1,83,719	19.9	3,37,704
Middle	23.3	1,64,343	21.1	1,88,752	22.1	3,53,095
Richer	26.2	1,66,409	22.5	1,90,920	24.2	3,57,329
Richest	29.8	1,60,836	24.8	1,85,012	27.1	3,45,847
Smoking or tobacco use						
No	22.4	4,76,082	20.3	8,38,898	21.1	13,14,981
Yes	26.8	3,08,509	30.7	83,616	27.6	3,92,125
Alcohol consumption						
No	22.7	6,32,474	21.1	9,10,500	21.7	15,42,973
Yes	30.2	1,52,011	30.7	12,024	30.2	1,64,035
Body mass index (BMI in kg/m^2)						
Normal (BMI 18.5–24.9)	15.9	54,684	9.4	3,79,292	10.3	4,33,976
Thin (BMI < 18.5)	8.0	13,911	5.9	1,21,729	6.1	1,35,640

Contd…

Contd…

Background characteristics	*Men*		*Women*		*Overall*	
	Prevalence of hypertension (%)	*Weighted sample*	*Prevalence of hypertension (%)*	*Weighted sample*	*Prevalence of hypertension (%)*	*Weighted sample*
Overweight (BMI 25.0–29.9)	30.3	16,957	19.2	1,14,894	20.6	1,31,851
Obese (BMI ≥ 30.0)	39.4	3,571	27.9	41,291	28.8	44,862
BMI not measured	24.9	6,96,488		44.9	2,65,424	
Waist circumference						
Normal (women: (≤ 80 cm); men (≤ 94 cm))	15.6	78,375		7.6	3,91,157	
Increased risk of metabolic complications (women: (> 80 cm); men (> 94 cm))	38.5	10,851		17.6	2,66,096	
Not measured	24.9	6,96,384		44.9	2,65,378	
Random blood glucose level						
Normal (≤ 140 mg/dl)	20.0	6,56,638		17.2	7,88,905	
High (> 140 mg/dl)	40.3	1,11,570		40.1	1,11,794	
Not measured	78.6	17,402		69.4	21,932	

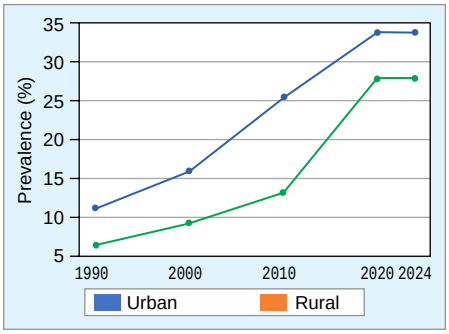


Fig. 1: Increasing trend in hypertension prevalence in India (urban vs rural, 1990–2024)[20]

century varied among different studies in India and ranged from 2 to 15% in Urban India and 2–8% in Rural India. The prevalence has increased over six decades to 22.6%, with the prevalence reaching 24.1% in men and 21.2% in women. The prevalence also increases with age, reaching 48.4% in individuals aged 60 and above.[19]

Rural/Urban Trends of Hypertension in India

Urban residents show a slightly higher prevalence (25%) of hypertension than rural residents (21.4%), indicating the rapid spread of hypertension across all populations. Thus, there has been a rural and urban convergence in the last two decades, as seen with other risk factors due to the changing lifestyle in rural areas. Various factors associated with economic progress might have contributed to this rising trend, such as increased life expectancy, urbanization, and its related lifestyle changes, including increasing salt intake. Another contributing factor may be the increased awareness and detection of hypertension (Fig. 1).[20]

Salt sensitivity, characterized by an individual's BP response to dietary sodium intake, significantly influences hypertension trends in India. Studies indicate that a substantial portion of both normotensive and hypertensive individuals in India exhibit salt-sensitive phenotypes.[20]

In northeastern India, a study involving 374 participants found that 40.8% of normotensive and 47.6% of hypertensive subjects were salt-sensitive. Notably, increased salt consumption was independently associated with salt sensitivity. Similarly, a study in the Kashmiri population reported significant reductions in BP following salt restriction, highlighting the prevalence of salt-sensitive hypertension in this demographic.

These findings underscore the importance of dietary salt intake in managing hypertension across various Indian demographics. Implementing community-wide salt reduction strategies could be a crucial step in addressing the hypertension epidemic in India.[20]

Demographic-based Hypertension Trends in India

The prevalence of hypertension steadily increases with age, with nearly 50% of people above the age of 60 years being hypertensive. The prevalence of hypertension is found to be higher in non-literate individuals (30.4%) and less in people with a higher level of education (17.0%). Hypertension also increases as the wealth index increases. People from the lowest wealth index are less hypertensive (19.0%) than people from the highest (27.1%).[20]

Hypertension is more prevalent among tobacco users (27.8%) than non-users (21.1%). Additionally, hypertension is found to be more prevalent among obese people with a BMI greater than or equal to 30 Kg/m^2 (28.8%) and less frequent in those with a lower BMI of less than 18.5 Kg/m^2 (6.1%).

Moreover, hypertension prevalence is high among persons with a higher waist circumference, indicative of an increased risk of metabolic complications (18.4%). Specifically, it is higher among men (38.5%) with a waist circumference above 94 cm and women with a waist circumference above 80 cm (17.6%) (Table 8).[17]

The prevalence of hypertension is found to be high (40.2%) among those who have a random blood glucose level above 140 mg/dL. A similar pattern of hypertension prevalence is found for both men (40.3%) and women (40.1%) among those who have a high random blood glucose level.

Regional Variation in Hypertension Prevalence in India

As per the National Family Health Survey (NHFS-5), the prevalence of hypertension (elevated BP >140 mm Hg systolic, >90 mm Hg diastolic or on current medications for hypertension) was recorded among rural and urban Indian populations across 636,999 households, including 7,85,611 men and 9,22,631 women (totally 17,08,241 people). The highest prevalence was seen in Sikkim and lowest in Dadra and Nagar Haveli and Daman and Diu, for both the urban and rural populations as well as for both genders. Further analysis of the present

Table 9: Prevalence of hypertension among men and women aged 15 and over, according to state/union territory, India, 2019–21

		Men		*Women*		*Overall*	
State code	*State name*	*Prevalence of hypertension (%)*	*Weighted sample*	*Prevalence of hypertension (%)*	*Weighted sample*	*Prevalence of hypertension (%)*	*Weighted sample*
–	India	24.1	7,85,611	21.2	9,22,631	22.6	17,08,241
1	Jammu and Kashmir	21.8	4,221	22.3	5,334	22.1	9,555
2	Himachal Pradesh	24.4	4,786	22.2	5,820	23.2	10,606
3	Punjab	37.9	17,093	31.1	19,628	34.2	36,721
4	Chandigarh	29.8	418	25.2	579	27.1	997
5	Uttarakhand	32.3	5,307	23.0	7,338	26.9	12,645
6	Haryana	25.3	15,976	21.0	18,133	23.0	34,109
7	NCT of Delhi	32.8	10,580	24.1	12,686	28.0	23,266
8	Rajasthan	17.9	49,200	15.3	57,232	16.5	1,06,431
9	Uttar Pradesh	21.8	1,20,851	18.3	1,47,465	19.9	2,68,317
10	Bihar	18.4	59,480	15.9	80,176	17.0	1,39,657
11	Sikkim	41.4	336	34.6	374	37.9	710
12	Arunachal Pradesh	33.2	683	24.9	730	28.9	1,413
13	Nagaland	29.5	682	23.7	730	26.5	1,412
14	Manipur	33.6	1,469	23.2	1,719	28.0	3,187
15	Mizoram	25.0	768	17.8	806	21.3	1,574
16	Tripura	23.1	2,731	21.1	2,972	22.0	5,702
17	Meghalaya	21.8	1,635	18.9	1,881	20.3	3,516
18	Assam	21.2	18,488	19.7	20,849	20.4	39,337
19	West Bengal	20.1	58,123	20.2	66,542	20.2	1,24,665
20	Jharkhand	22.4	20,732	17.7	24,540	19.9	45,272
21	Odisha	25.6	27,723	22.3	33,843	23.8	61,566
22	Chhattisgarh	27.6	21,432	23.5	23,156	25.5	44,589
23	Madhya Pradesh	22.5	48,164	20.4	53,621	21.4	1,01,785
24	Gujarat	20.1	45,240	20.3	46,424	20.2	91,664
25	Dadra and Nagar Haveli and Daman and Diu	17.2	275	16.4	262	16.8	537
27	Maharashtra	24.1	79,139	22.7	86,757	23.4	1,65,896
28	Andhra Pradesh	29.2	33,584	25.4	38,992	27.2	72,576
29	Karnataka	28.6	38,901	26.0	45,642	27.2	84,542
30	Goa	35.9	454	32.0	655	33.6	1,110
31	Lakshadweep	24.9	49	24.7	64	24.8	113
32	Kerala	32.3	21,898	30.1	28,555	31.1	50,452
33	Tamil Nadu	30.1	54,849	24.8	64,821	27.2	1,19,670
34	Puducherry	30.1	849	22.8	1,021	26.1	1,870
35	Andaman & Nicobar Islands	29.7	275	24.9	279	27.3	554
36	Telangana	31.5	19,127	26.1	22,894	28.6	42,021
37	Ladakh	19.9	93	17.5	109	18.6	202

study highlighted that the top five states with highest prevalence are Sikkim, Punjab, Arunachal Pradesh, Kerala, and NCT of Delhi (Table 9 and Fig. 2).[17]

India: Special Feature of Hypertension

Hypertension in India has some special features such as onset occurring relatively early in life, a rural-urban divide in prevalence, clustering of multiple cardiovascular risk factors and a significant seasonal variation of BP (Table 10).

Control and Awareness of Hypertension in India

As per a recent survey by Grover et al, the awareness of hypertension among the surveyed population was only 50.5%. The rate of awareness was lower in men (34.7%) compared to women (53.6%). Similarly, among those aware of their hypertensive status, more women had blood pressure under control (74.6%) as compared to men (61.7%) (Fig. 3).

Additionally, awareness of hypertension increased with the level of education, primary vs secondary schooling. Participants in the poor and middle wealth quartile were 60% and

Table 10: Hypertension in India–special features[17]

1. Onset early in life
2. Rural-urban divide in prevalence
3. Clustering of multiple CV risk factors
4. Significant seasonal variation of BP
5. Rising average BP of general population
6. Low awareness, treatment and control rates
7. Early HMOD–possibly due to poor control

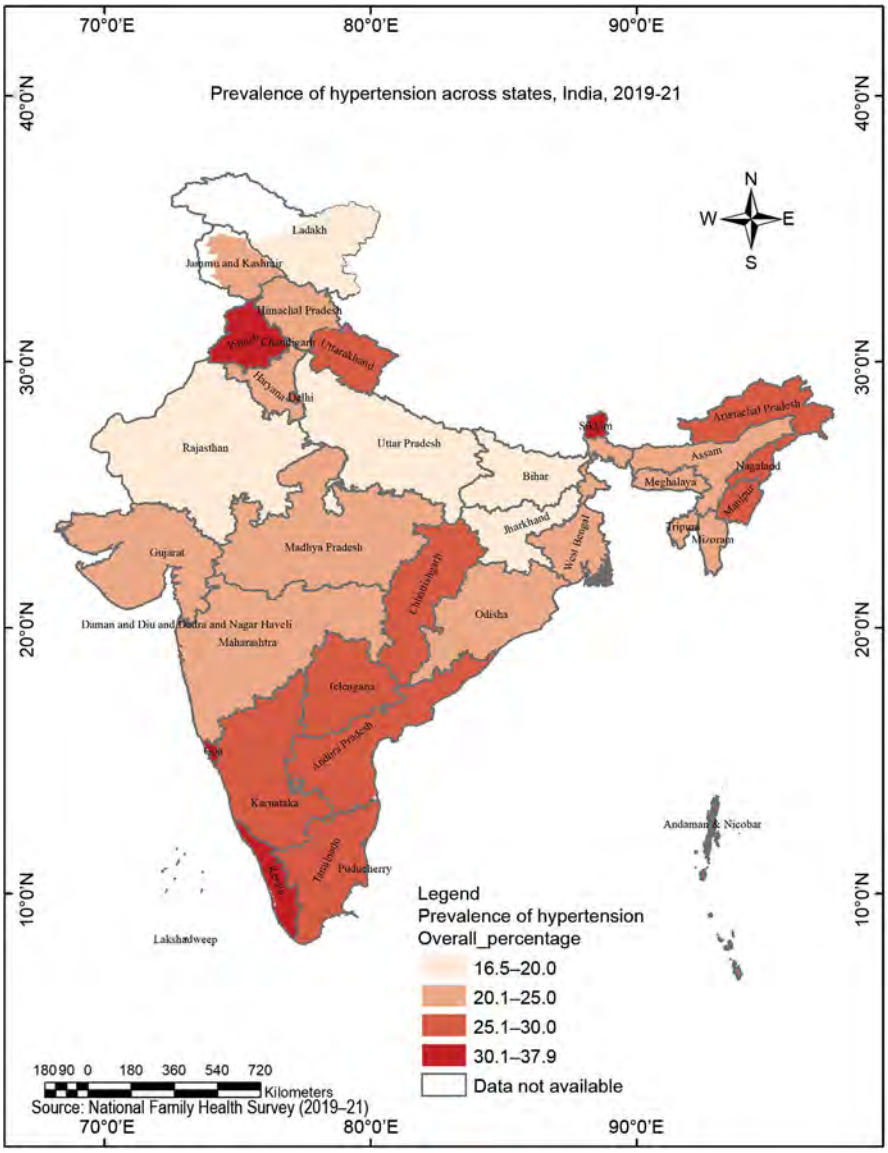


Fig. 2: Prevalence of hypertension across states, India, 2019–21[17]

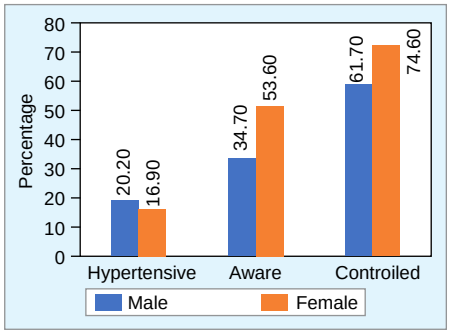


Fig. 3: Prevalence of hypertension, awareness, and control by gender[17]

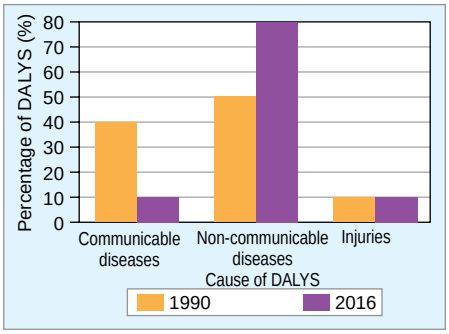


Fig. 4: Leading causes of DALYs in 1990 and 2016 (shift from communicable to noncommunicable diseases)[19]

48% less likely to be aware of hypertension, respectively than those in the highest quartile.

In this cross-sectional survey study of Indian adults from 1999 to 2021, more than 1 in 4 people were found to have hypertension, and of these, only 1 in 3 received a diagnosis, less than 1 in 5 were treated, and only 1 in 12 had BP under control. National mean values hide considerable state-level and district-level variations in the care continuum, suggesting the need for targeted, decentralized solutions to improve the hypertension care continuum in India.[17]

Table 11: Increasing trends in deaths and disability-adjusted life years (DALYs) due to high systolic blood pressure in India

Year	*Deaths (millions)*	*DALYs (millions)*
2000	0.91	14.5
2005	1.1	17.3
2010	1.25	19.5
2015	1.45	22.0
2020	1.65 (estimated)	24.8 (estimated)
2024	1.85 (estimated)	27.5 (estimated)

India's Burden of Hypertension and Cardiovascular Disease

India's burden of hypertension is compounded by a high burden of cardiovascular diseases (CVDs). In 2016, the total number of deaths from CVDs in India was estimated to be over 2.5 million, with the majority attributed to coronary artery disease (CAD) and strokes. The rise in CVD mortality parallels the increase in hypertension prevalence, with hypertension being a key risk factor for both CAD and cerebrovascular accidents (CVA).[17]

Hypertension is a significant contributor to premature death in India, with the Indian Council of Medical Research (ICMR) estimating that hypertension is responsible for 16% of ischemic heart disease (IHD), 21% of peripheral artery disease (PAD), 24% of acute myocardial infarction (AMIs), and 29% of stroke cases (Fig. 4 and Table 11).[18]

Hypertension and Healthcare Costs

The treatment of hypertension is usually lifelong, although the downregulation of therapy can be achieved in some cases. The cost of therapy assumes great relevance for hypertension therapy. India spends only 3.83% of its GDP on health, and the per capita health expenditure was only Rs. 6,602 in 2021–2022, which is much lower than in other nations. Since universal health care coverage is still not available for all patients, the cost of medicines is an important issue for improving long-term drug compliance in our country, as 80–100% of the population has insurance coverage in most Western countries.[18–22]

Conclusion

Nearly one in every fifth Indian is hypertensive, and this number is relentlessly increasing. Hypertension is more prevalent in the elderly, in people residing in urban areas, non-literate people, those with the richest wealth index, those with higher BMI, those with higher blood glucose and those who are tobacco users and consume alcohol. This positive correlation highlights the need for public health interventions to implement targeted and adequate preventive health measures in our country.

Measurement of Blood Pressure

Clinic (Office) Blood Pressure Measurement

- Blood pressure can exhibit large spontaneous variations; therefore, the diagnosis of hypertension should be based on multiple BP measurements obtained across several separate occasions.
- With increasing awareness about the hazardous effects of mercury on health, the mercury sphygmomanometer should be discontinued. We recognize that mercury is a potent toxin, a global priority pollutant, and a persistent bioaccumulative agent. A mercury sphygmomanometer contains 70 to 90 grams of mercury.[23] Organizations like Health Care Without Harm (HCWH) and the WHO are together leading a global partnership to achieve the virtual elimination of mercury-based thermometers and sphygmomanometers.
- Humans are exposed to methylmercury almost entirely through the consumption of contaminated fish, seafood, and wildlife that are at the top of the aquatic food chain. It is recommended that physicians should phase out the mercury sphygmomanometers and replace them with aneroid and digital oscillometric devices. Some mercury sphygmomanometers can be kept only for the purpose of calibration.
- The aneroid large dial apparatus is the best for use in the office. It needs calibration every six months since the spring can loosen. Proper maintenance and calibration of the sphygmomanometer should be performed regularly. The automated office blood pressure (AOBP) equipment has been used recently in the SPRINT trial.[15] These are not cost-effective and may not be feasible as the devices of choice. The aneroid and the digital oscillometric sphygmomanometers should be used.
- Use a standard cuff with a bladder that is 12 cm × 35 cm. A larger bladder should be used for individuals with a larger arm circumference, and a small bladder should be used for children. The bladder should encircle and cover at least 80% of the circumference of the upper arm. For measurement, inflate the bladder quickly to a pressure 20 mm Hg higher than the point of disappearance of the radial pulse. Deflate the bladder slowly by 2 mm Hg every second. The first appearance of the sound (Phase I Korotkoff) is the systolic BP. The disappearance of the sound (Phase V Korotkoff) is the diastolic BP. For children and in those with high output states, muffling of the sound (Phase IV Korotkoff) is taken as diastolic pressure (Fig. 5).

Precautions

The following precautions should be taken for the correct measurement of blood pressure:

- At the initial visit, an average of three readings, taken at intervals of 2–3 minutes, should be recorded.
- For confirmation of diagnosis of hypertension, record at least three sets of readings should be recorded on different occasions, except in Stage III hypertension.
- Patients should be asked to refrain from smoking, drinking tea/ coffee or exercising for at least 30 minutes before measuring the BP.
- Allow the patient to sit for at least five minutes in a quiet room before beginning BP measurement.
- Measurements should be obtained while the patient is in a sitting position. The patient's arm should be fully bare and supported at the level of the heart.
- Measure the blood pressure in both arms at the first visit and use the higher of the two readings.
- In older persons aged 60 years and above, in diabetic patients, and patients on antihypertensive therapy, the BP should be measured in both supine/sitting and standing positions to detect postural hypotension.
- If atrial fibrillation is present, additional readings may be required to estimate the average SBP and DBP.
- Occasionally, thigh BP (popliteal) has to be measured with an appropriately large cuff, with the patient in prone position, especially for younger persons with hypertension. Normally, thigh SBP is higher and DBP a little lower than the arm BP values because of the reflected pulse wave. This is important for suspected coarctation of aorta and nonspecific aorto-arteritis, where BP values are lower in the lower limb as compared to the upper limb.

Key Points

- The room should be calm and quiet.
- The patient should not have smoked or consumed anything 30 min before the measurements.
- The patient's bladder should be empty.
- The patient should sit comfortably for 5 min before the BP measurement.
- The patient should not talk or move.
- The patient's legs should not be crossed.
- The patient's back should be supported.
- The cuff should fit properly (not too loose/ not too tight).
- The cuff placement should be correct, specifically 2–3 cm above the elbow fossa.
- The arm should be supported at the level of the heart.
- Equipment should be calibrated.
- The cuff should be inflated, and the BP should be recorded thereafter (Fig. 6).

Summary of Office Blood Pressure Measurement

A summary of office blood pressure measurement is shown in Figure 7.

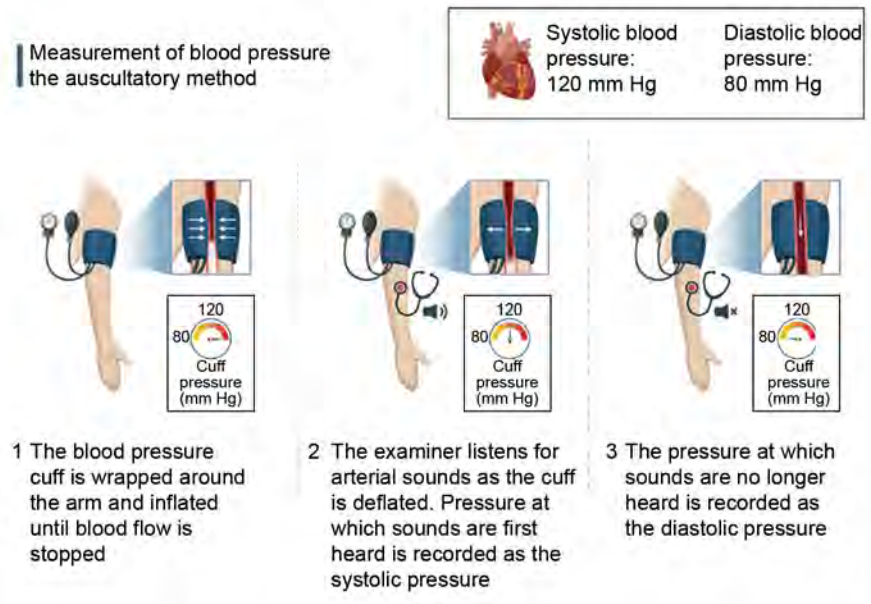


Fig. 5: Measurement of blood pressure (auscultatory method)

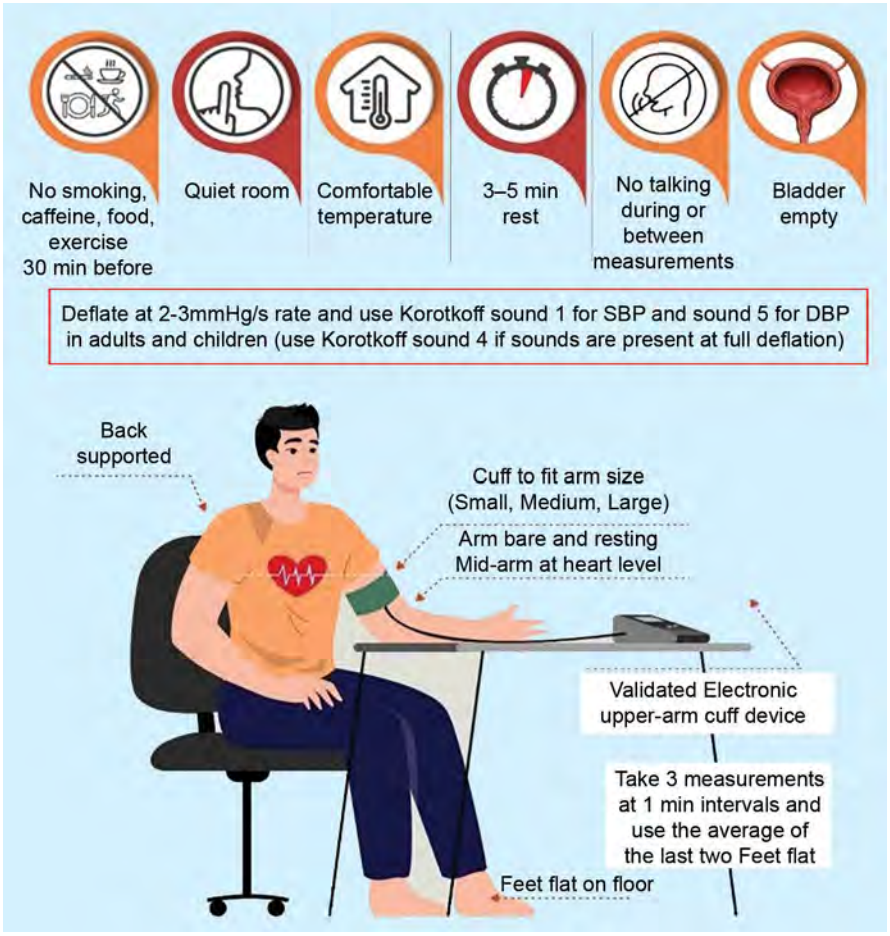


Fig. 6: Blood pressure measurement: key precautions (Courtesy: International Society of Hypertension Guidelines, 2022)

Table 12: Blood pressure cuff size selection based on arm circumference

Arm circumference	*Cuff*	*Size*
22–26 cm	12 × 22 cm	Small
27–34 cm	16 × 30 cm	Medium
35–44 cm	16 × 36 cm	Large
45–52 m	16 × 42 cm	Extra-large

Self-monitored Blood Pressure Measurement/Home Blood Pressure Measurement

Measurement of BP outside the clinic may provide valuable information for the initial evaluation of patients with hypertension and for monitoring the response to treatment. Home measurement can distinguish sustained hypertension from "white-coat hypertension," a condition noted in patients whose BP is elevated in the physician's clinic but normal at other times.

Validated automated (oscillometric) machines that use the brachial artery (arm) for measurement are reliable, whereas finger and wrist monitors are inaccurate and are not recommended. Importantly, the oscillometric devices may not work reliably in patients who have atrial fibrillation or other arrhythmias.

Technique

- Caffeine, smoking, alcohol, bathing, and exercise should be avoided for at least 30 minutes before the reading is taken.
- The patient should sit calmly with the back support, feet flat on the floor for 5 minutes before taking a reading. The upper arm should be bare. When taking a reading the arm with the cuff should be supported on a firm surface (table or armrest) at the heart level. The cuff should fit snugly on the arm, about 0.5 -1 inch above the elbow crease.
- Readings should be taken in the morning before medication and at night. Each time, two readings should be taken at an interval of one to two minutes. Moreover, readings should be taken twice a day for 7 consecutive days. The readings of the first day should be discarded. The average of the remaining 12 readings is considered the home blood pressure measurement.
- For home BP, readings of more than 135/85 mm Hg should be considered as elevated BP.
- Self-monitored/home BP monitoring (HBPM) is easy to perform, reproducible, and is more effective at predicting target organ damage than clinic BP measurement. It can be used to distinguish white-coat hypertension from sustained hypertension. The HBPM improves compliance and ensures better BP control. We recommend the use of this modality after proper patient education. The patient should be educated not to change their medication without consulting their physician.

Methodology

Measurement of BP

- Patient should not smoke or consume tea, coffee, or other caffeinated products 30 minutes before BP measurement.
- Patient should relax for at least 5 minutes before the measurement of the BP.
- Patient should not talk during the BP measurement
- Patient should always sit properly with back support.
- Patient's legs should not be crossed.
- The cuff should be placed on the arm correctly.
- The arm should be supported at the level of the heart.

Recording of BP

- The patient should record their BP within 1 hour of awakening (after urination and before breakfast) and before going to bed in the evening.
- The patient should record their BP and the timing of measurement.
- The patient should obtain 2 consecutive measurements at least 1 minute apart.
- The patient should record BP 2 times a day (once in the morning and once in the evening)
- The patient should record BP for at least 4 days and preferably for 7 days.

Calculating Blood Pressure

- The measurement recorded on the first day should be discarded.
- The average of all remaining readings should be calculated (at least 12 readings).

Selection of Cuff

- The selection of the cuff should be based on arm circumference, cuff length, cuff width, body type, cuff size, etc.
- *Arm circumference*: Measure the circumference of your upper arm at its midpoint.
- *Cuff length*: The inflatable part of the cuff should cover 75–100% of the upper arm's circumference.
- *Cuff width*: The cuff should cover 40–80% of the distance from the elbow to the shoulder.

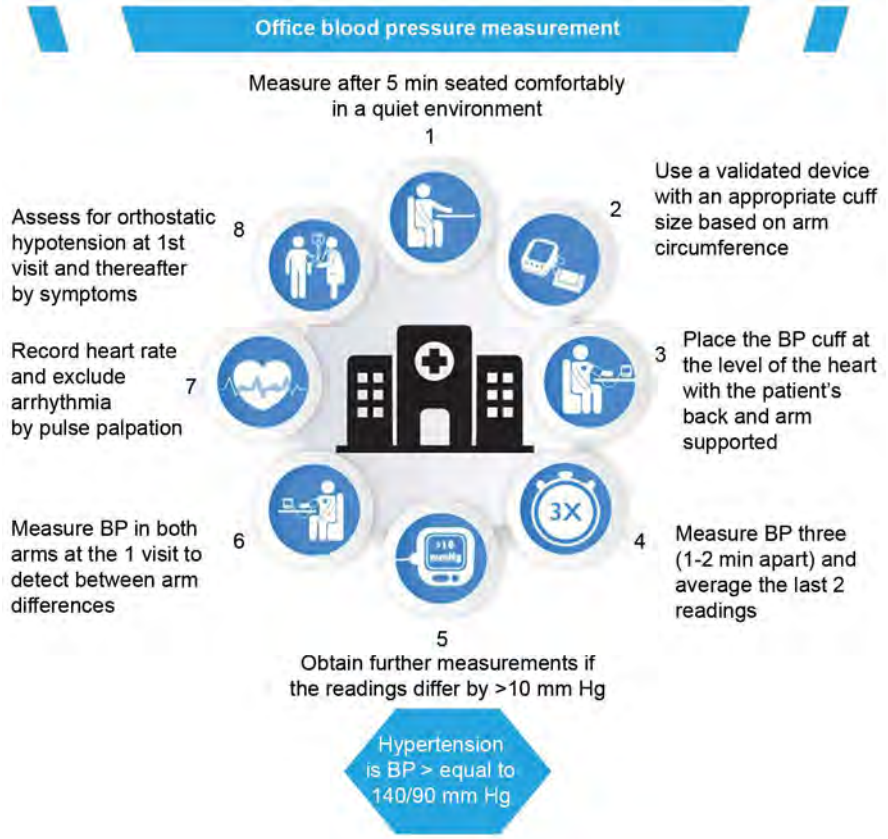


Fig. 7: Office blood pressure measurement

Table 13: Factors influencing BP readings

Patient/physician-related factors	*Factors*	*BP (increase/decrease)*
Patient	Caffeine intake	10 mm Hg
Patient	Distended urinary bladder	10–15 mm Hg
Patient	Speaking	7–10 mm Hg
Patient	Active Listening	5 mm Hg
Patient	Legs crossed	2–8 mm Hg
Patient	Smoking	6 mm Hg
Patient	Lack of back support	6–10 mm Hg
Physician	Cuff over clothes	5–50 mm Hg
Physician	Smaller cuff	10 mm Hg
Physician	Positioning of the bladder	If the cuff is placed above the level of the heart, BP will increase by 2 mm Hg for every inch above heart level.

- *Body type*: Obese patients need longer, wider cuffs to compress the brachial artery.
- *Cuff size for children*: The cuff bladder width should be at least 40% of the arm circumference halfway between the olecranon and acromion (Tables 12 to 14).

Summary of Self-monitored Blood Pressure Measurement

The summary of self-monitored blood pressure measurement is shown in Figure 8.

Ambulatory Blood Pressure Monitoring (ABPM)

At least 20–25% of patients diagnosed with stage I-II hypertension (DBP 90–104 mm Hg) are normotensive outside the physician's clinic. ABPM is a method of measuring BP over a 24-hour period and is considered the most accurate method for BP measurement.

Ambulatory blood pressure monitoring (ABPM) has been found to be clinically useful for identifying white-coat hypertension, masked hypertension, nocturnal hypertension (non-dippers), resistant hypertension and episodic hypertension (Fig. 9). It has been proven valuable for evaluating the effect of antihypertensive drugs and for monitoring hypotensive episodes in patient already on antihypertensive medication.

For measuring ambulatory BP, a portable monitor is worn on a belt connected to a standard cuff on the upper arm. BP measurements are taken over a 24–48-hour period every 15–20 minutes during the daytime (8 am to 10 pm) and every 60 minutes during nighttime.[24,25]

BP shows a reproducible circadian profile, with higher values while awake and mentally and physically active, whereas much lower values during rest and sleep. Different values have been suggested for the definition of hypertension with ABPM for daytime average BP (>135/85 mm Hg) and the nighttime average (>120/70 mm Hg) (Table 2).

The early morning surge in BP for 3 or more hours during transition from sleep to wakefulness can be an independent risk factor and needs to be managed effectively,[26] by addition of a second dose in the evening or a dose of a second class of

Table 14: BP variations in various scenarios and situations

Activities	*Systolic BP (mm Hg)*	*Diastolic BP (mm Hg)*
Meeting	20	15
Working	16	13
Walking	12	5.5
Wearing clothes	11.5	9.7
House chores	10.7	6.7
Phone calls	9.5	7.2
Talking	6.7	6.7
TV watching	0.3	1.1
Resting	0	0
Sleeping	–10	–7.6

Table 15: Patterns of nocturnal BP variations on ABPM (change in the nighttime BP compared to the daytime BP)

Dipping (Physiological)	10–20% decline in nighttime BP
Nondipping	<10% decline in nighttime BP
Extreme Dipping	>20% decline in nighttime BP
Reverse Dipping	No drop / Increase in nighttime BP

Table 16: Key differences between the ABPM and self-monitoring of BP (SMBP)

ABPM	*SMBP*
Identifies hypertension in the clinic and out of the clinic	Identifies hypertension in the clinic and out of the clinic
Prognostic importance is high	Mainly used by patients
Records nocturnal BP	BP is recorded mainly during day
Records BP over a 24-hour period	BP level is obtained at a particular time
BP variability can be assessed easily	BP variability can be assessed over long-term measurements
Only available in hospital settings	Can be performed by the patients at home
Records BP during every activity	Records only static BP
Additional BP phenotyping (e.g., nocturnal dipping status)	Allows patient engagement in BP measurement and shows telemedicine potential
Relatively expensive and sometimes has limited availability	Cheap and widely available
Can be uncomfortable and affect sleep	Potential for measurement errors due to improper measurement techniques

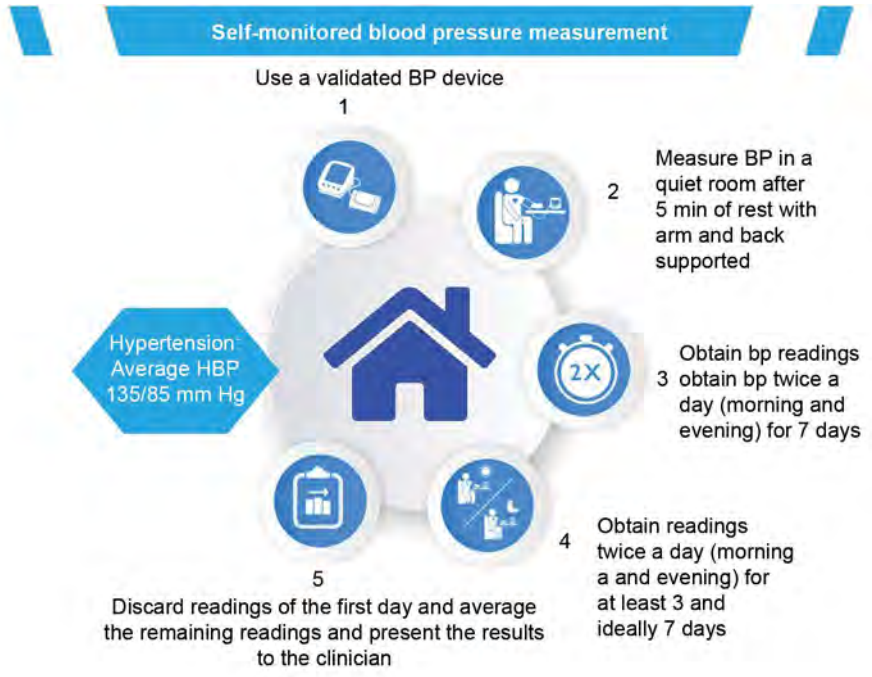


Fig. 8: Self-monitored blood pressure measurement

antihypertensive agent in the evening, or a drug with a longer half-life.

The data recorded from ABPM also identifies patterns of nocturnal blood pressure variation such as dipping, nondipping, extreme dipping, and reverse dipping (Table 15). The nighttime blood pressure is normally 10–20% less than the daytime blood pressure. This physiological pattern is called dipping. Patterns of non-dipping and extreme dipping are associated with increased cardiovascular and cerebrovascular event rates. In the case of reverse dipping, a diagnosis of obstructive sleep apnea should be considered. Notably, ABMP is a better predictor of cardiovascular events and all-cause mortality than clinic BP measurement (Fig. 9 and Table 16).

Clinic BP	Mean 24-hour ambulatory BP: <130/80	Mean 24-hour ambulatory BP: >130/80
>140/90	White coat hypertension	Sustained hypertension
>140/90	True normotension	Masked hypertension

Fig. 9: Classification of blood pressure based on clinic and ambulatory blood pressure measurements

Indication for ABPM

- White coat hypertension.
- Nocturnal hypertension.
- Masked hypertension.
- Resistant hypertension.
- Special conditions like elderly patients, diabetes, and pregnancy.
- Signs of HMOD in normotensive patients.

Summary of Ambulatory Blood Pressure Measurement

The summary of ambulatory blood pressure measurement is shown in Figure 10.

Pulse Pressure

The pulse pressure (SBP–DBP) depends upon factors like arterial stiffness (the cushioning capacity of arteries) and wave reflections, the speed of the forward wave (pulse wave velocity or PWV).

MBP is the pressure associated with the steady flow of blood to peripheral tissues. PP is the consequence of intermittent ventricular ejection from the heart and is influenced by the left ventricular ejection fraction and large conduit arteries, mainly the aorta. Factors like arterial stiffness (the cushioning capacity of arteries) and

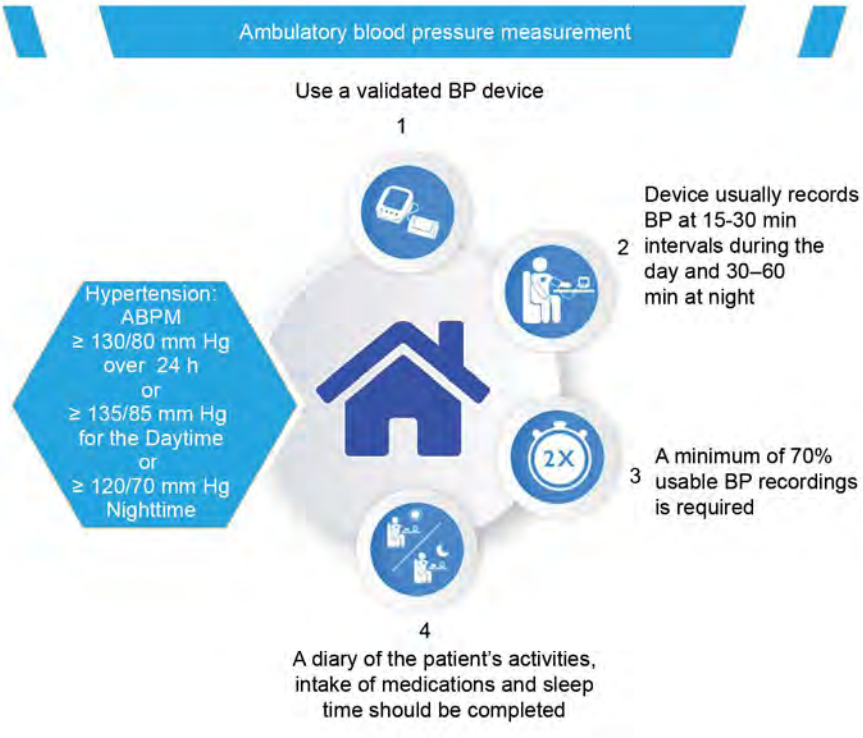


Fig. 10: Ambulatory blood pressure measurement

wave reflections–speed of the forward wave (pulse wave velocity or PWV) are also major determinants of PP. In subjects >50 years of age, the arterial stiffness and wave reflections become the main determinants of increased SBP and PP.

Novel methods of monitoring central aortic pressure are being developed. The therapeutic approaches available to reduce PP and arterial stiffness with age are ACEIs or ARBs in association with CCBs and/or diuretics.

Evaluation and Risk Assessment of Blood Pressure

Evaluation

- Evaluation of patients with documented hypertension serves three primary objectives:
- To identify known causes of high BP.
- To assess the presence or absence of hypertension-mediated organ damage (HMOD).
- To identify other cardiovascular (CV) risk factors or concomitant disorders that may define prognosis and guide treatment.

Data for evaluation are gathered based on medical history, physical examination, laboratory tests, and special diagnostic procedures.

Medical History

- Duration and level of elevated BP, if known.
- Symptoms of coronary artery disease (CAD), heart failure, cerebrovascular disease, peripheral vascular disease, and chronic kidney disease (CKD).
- Diabetes mellitus, dyslipidemia, obesity, gout, sexual dysfunction, and other co-morbid conditions.
- Family history of hypertension, obesity, premature CAD, stroke, dyslipidemia, and diabetes.
- Symptoms indicative of secondary causes of hypertension.
- History of smoking or tobacco use, physical activity, dietary assessment (including sodium, alcohol, saturated fat, and caffeine intake), and history of sleep patterns and sleep-related disorders.
- Socioeconomic, professional, and educational background.
- Current use of prescribed and over-the-counter medications, herbal remedies, licorice (Yashtimadhu/Jestamadha), illicit drugs, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), or nasal drops, which may raise BP or interfere with antihypertensive drugs.
- Oral contraceptive use and history of hypertension during pregnancy.
- History of previous antihypertensive therapy and any associated adverse effects.
- Level of adherence to antihypertensive therapy.
- Psychosocial and environmental factors.

Physical Examination

- Record three BP readings, at intervals of 2 minutes, with the patient supine or sitting and after standing for 2 minutes.
- Measure height, weight, BMI, and waist circumference.
- Examine the pulse and extremities for delayed or absent femoral/peripheral pulses, bruits, and pedal edema.
- Check for physical signs such as arcus senilis, acanthosis nigricans, xanthelasma, and xanthomas.
- Examine the neck for carotid bruits, raised jugular venous pressure, or thyroid gland enlargement
- Assess the heart for rate, rhythm, apex beat location, murmurs, or fourth heart sound.
- Examine the lungs for crepitations or rhonchi.
- Palpate the abdomen for bruits, enlarged kidneys, masses, or abnormal aortic pulsations.
- Perform optic fundus examination and neurological assessment.

Laboratory Investigations

Routine Tests

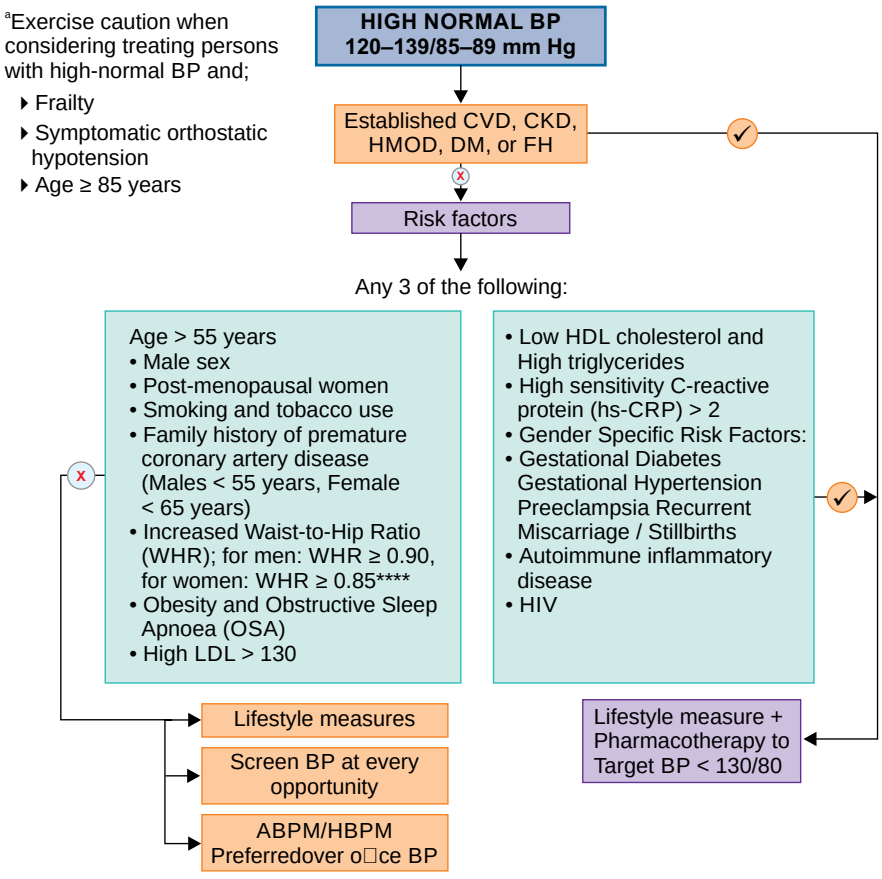
- Urine examination for protein, glucose, and microscopic evaluation for RBCs and other sediments.
- Hemoglobin, fasting blood glucose, serum creatinine, potassium, and total cholesterol.
- 12-lead electrocardiogram.

Additional Tests (Special Circumstances)

- Fasting lipid profile and uric acid.
- Urine albumin–creatinine ratio.
- Echocardiogram.
- Abdominal ultrasound.
- Carotid intima media thickness test (CIMT).
- Ankle brachial index.

Specific Tests (Secondary Hypertension)

- Tailored to the suspected underlying cause.



****WHR ≥ 0.90 for men and WHR ≥ a 0.85 women are considered as makers for abdominal obesity as per Indian metabolic syndrome guidelines.
Thes values are associated with increased risk of metabolic disorders and cardiovascular diseases.

Fig. 11: Algorithm of risk-based approach to blood pressure treatment in adults

Table 17: Factors influencing risk of cardiovascular diseases

Risk factors for coronary artery disease (RF)	*Hypertension-mediated organ damage (HMOD)–subclinical*	*Associated clinical conditions (ACC)*
Age > 55 years*	Left ventricular hypertrophy detected by ECG and/or echocardiogram	Diabetes mellitus
Male sex	Moderately increased albuminuria[#]/proteinuria and/or reduced eGFR [eGFR 60–90 mL/min/1.73 m^2, elevated urinary albumin creatinine ratio (ACR)[‡]]	Cerebrovascular disease (transient ischemic attack, ischemic stroke, cerebral hemorrhage)
Post-menopausal women	Ultrasound or radiological evidence of atherosclerotic plaques in carotids or femorals	Heart disease (acute coronary syndrome, chronic coronary syndrome, coronary revascularization, heart failure)
Smoking and tobacco use	Hypertensive retinopathy	Renal disease [diabetic kidney disease, chronic kidney disease (eGFR <60 mL/min/1.73 m^2)]
Family history of premature coronary artery disease (men < 55 years, women < 65 years)	Ankle brachial index (< 0.9)	Vascular disease (peripheral arterial disease, including nonspecific aortoarteritis, aortic dissection)
Increased waist-to-hip ratio (WHR) (for men: WHR ≥ 0.90, for women: WHR ≥ 0.85)[†]	Coronary artery calcium score (CAC > 100 Agaston units) on cardiac CT	Advanced hypertensive retinopathy (hemorrhages or exudates, papilledema)
Obesity and obstructive sleep apnea (OSA)	Elevated high-sensitivity cardiac troponin levels**	Familial hypercholesterolemia
High LDL > 130 mg/dL	Elevated NT-proBNP levels[##]	
Low HDL cholesterol and high triglycerides	Large artery stiffness (carotid–femoral or brachial–ankle pulse wave velocity)	
High sensitivity C-reactive protein (hs-CRP) > 2		
Gender-specific risk factors (gestational diabetes, gestational hypertension, preeclampsia, recurrent miscarriage/stillbirths)		
Autoimmune inflammatory disease		
HIV		

*Coronary artery disease is known to occur 10 years earlier in South Asians than in other ethnic groups; [#]Moderately increased Albuminuria (Microalbuminuria) 30–300 mg/24hours; [‡]Albumin-Creatinine Ratio (ACR) ≥22 mg/g creatinine for men or ≥31 mg/g creatinine for women; [†]WHR ≥ 0.90 for men and WHR ≥ 0.85 for women are considered as markers for abdominal obesity as per the Indian Metabolic Syndrome Guidelines. These values are associated with an increased risk of metabolic disorders and CV diseases; **hs-cTnT–Normal range: <14 ng/L, hs-cTnI–Normal range: <26 ng/L. hs-cTnT ≥ 14 ng/L and hs-cTnI ≥ 26 ng/L suggest myocardial injury. These levels must be interpreted in conjunction with clinical symptoms and other diagnostic tests; [##]NT-proBNP: Normal levels: <125 ng/L for individuals aged <75 years; <450 ng/L for individuals aged 75 years or older; Elevated levels: ≥ 400 ng/L are associated with heart failure, especially in individuals aged ≥75 years. Age-related variation is critical for accurate interpretation

In certain cases, hs-CRP levels and moderately increased albuminuria may assist with risk stratification. Cost constraints should guide the necessity and extent of investigations, particularly in patients with essential hypertension and limited resources. Initiating therapy without laboratory investigations may be justified under such circumstances.

Factors Influencing Risk[5]

The overall CV risk prediction has been suggested in some of the latest guidelines for the initiation of therapy at lower BP levels.

Recent ESC and AHA guidelines emphasize the incorporation of overall CV risk in hypertension management. The American guidelines utilize pooled cohort equations for calculating 10-year atherosclerotic cardiovascular disease (ASCVD) risk, while the European guidelines rely on the Systemic Coronary Risk Evaluation (SCORE) system.

Currently, no risk scoring system is tailored specifically for Indian population. However, European guidelines estimate a 1.4-fold increased risk for South Asians due to a genetic predisposition to ASCVD at equivalent levels of risk factors. Observations suggest that existing global risk calculators underestimate CV risk in Indian patients.

Primarily, age, sex, lipids, diabetes mellitus, and smoking habit are the five major factors in all these risk score calculation systems. We should recognize the presence of these factors along with the fact that we Indians are genetically at a higher risk for ASCVD with any given level of these risk factors.

Besides risk calculated based on these factors or scoring systems, the other two factors affecting the overall risk of an individual are the presence of HMOD and other associated clinical conditions (ACC). The presence of one of these three factors would decrease the threshold for the initiation of drug therapy even at lower levels of BP. The prognosis of the patients and the choice and need for urgent therapy will be dependent on the overall risk stratification, as shown in Table 17 and Figure 11, based on the ASCVD risk, HMOD, and associated clinical conditions (ACC), respectively.

Management of Hypertension

Goals of Therapy

The main objective of hypertension treatment should be to control BP effectively to prevent, reverse, or delay complications, thereby minimizing the overall risk to the individual while ensuring that quality of life remains unaffected. Patients should be advised that lifestyle modifications and treatment adherence are usually lifelong, and regular drug compliance is mandatory.

Treatment Initiation

- After initial and overall risk profile assessments in patients, the following steps for managing hypertension should be followed.[4–6]
- Screening of BP should be done periodically (every 2–3 years) in patients below the age of 40 and every year in patients above the age of 40.
- BP must be recorded in both arms in lying and standing positions before initiating pharmacotherapy.
- For patients with optimal or normal BP (<130/85 mm Hg), lifestyle modifications should be encouraged, and BP screening should be continued.
- For patients with high normal BP (130–139/85–89 mm Hg) and high-risk conditions (established CVD, CKD, diabetes mellitus, familial hypercholesterolemia, HMOD) or more than three risk factors (RF), lifestyle modifications should be instituted, and early pharmacotherapy should be initiated to aim for a BP target of <130/80 mm Hg (Table 18).
- Lifestyle modification should be instituted immediately along with pharmacotherapy (monotherapy or low-dose double combination therapy) for patients with stage 1 hypertension. Lifestyle interventions for BP reduction are presented in Table 19.
- For patients with stage II or III hypertension, lifestyle modification should be instituted immediately along with pharmacotherapy (double or triple combination therapy). Frequent follow-up is recommended only until BP is controlled, especially in stage III patients, and repeated readings every few hours are highly suggested.
- In patients with evident high-risk conditions (established CVD, CKD, diabetes mellitus, familial hypercholesterolemia, HMOD), pharmacotherapy should be initiated as early as possible (Fig. 12).
- The combination of lifestyle modifications and pharmacological therapy should be followed duly, and patients must be counseled about the fact that lifestyle modifications may facilitate subsequent discontinuation or down-titration of medication. Following treatment therapy, patients should be advised to visit a general practitioner (GP) or a specialist every 1–3 months.[5]

Treatment Targets

The recommended BP levels for individuals below 60 years are 130/80 mm Hg, and for those above 60 years, the range should be between 130–140/80–90 mm Hg. The physiological age should be considered over the chronological age in the elderly. For active patients, the targets have to be implemented more vigorously. For frail patients, elderly patients (age >85 years), and patients with postural hypotension, a higher BP threshold can be considered.

The BP control targets should not be less than 120/70 mm Hg, as lower measurements are linked to greater risks. Given the significant variability of BP readings in any given individual, one should aim at maintaining most readings in the target range, while acknowledging that occasional values would be above or below this range. Overall, it is important to individualize these guidelines based on age, frailty, and the presence of other medical conditions and treatments (Table 20).[4–6]

Management Strategies

- Scientific evidence suggests a significant association between aging, elevated systolic BP, and pulse pressure, and the incidence of cardiac and vascular diseases.[5]
- A stronger correlation exists between SBP management and the reduction of mortality than the level of DBP control.[5,27–31]
- Epidemiologically, isolated systolic hypertension is the most common form of hypertension and is present in approximately two-thirds of hypertensive individuals >60 years of age.[5] SBP increases with age due to various factors including plaque accumulation, arterial stiffness, and a higher incidence of CVD.[32] Several studies suggest that systolic BP is a good predictor of CV health as age advances, whereas DBP is more indicative of CVD at younger ages.[32,33] Diastolic hypertension

Table 18: Blood pressure levels: treatment thresholds and target ranges

Category	*Threshold to initiate Treatment (mm Hg)*	*Target Blood Pressure Range (mm Hg)**
Age		
Below 65 years (High risk conditions/HMOD[+])	≥130/85	≤130/80
Below 65 years (No high-risk conditions / HMOD)	≥140/90	≤130/80
Between 65 and 80 years	≥140/90	130–140/70–80 (as per clinical judgment)
Above 80 years	140–150/90	130–140/70–80 (as per clinical judgment)

*BP levels should not be less than 120/70 mm Hg.

Table 19: Lifestyle modifications for blood pressure reduction

Intervention	*Recommendations*	*Estimated BP reduction*
DASH eating plan	Consume a diet abundant in fruits, vegetables, and low-fat dairy products, while limiting saturated and total fats	8–14 mm Hg
Sodium reduction	Limit daily sodium intake to less than 100 mmol (<2.4 g sodium or <6 g salt)	2–8 mm Hg
Physical activity	Engage in regular aerobic exercise, such as brisk walking, for at least 30 minutes on most days	4–9 mm Hg
Alcohol moderation	Abstinence is ideal; if consuming alcohol, limit to ≤21 units per week for men and ≤14 units per week for women	2–4 mm Hg
Tobacco use	Complete cessation is strongly advised	—
Adequate sleep and sleep hygiene	7–8 hours per day, with adequate duration and quality of sleep	—

DASH, Dietary approaches to stop hypertension.

predominates before 50 years of age, either alone or in combination with SBP elevation. Therefore, DBP is a more potent CV risk factor than systolic BP until age 50; thereafter, systolic BP should be considered as the prime factor.[34]

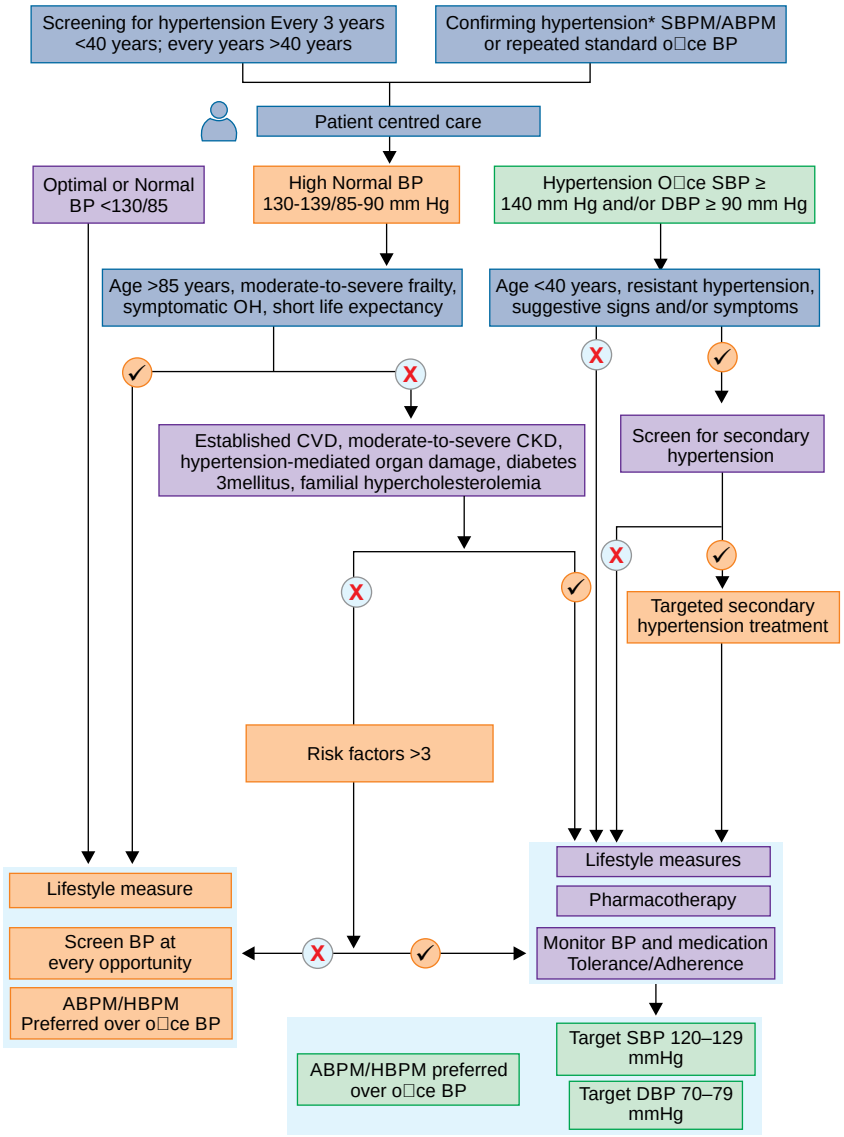


Fig. 12: Blood pressure control algorithm (Y, yes; N, no; *Mild hypertension should be confirmed based on ABPM or self-monitored blood pressure; ** Refer to Table 26 on risk factors)

- Trials describe population averages for the purpose of developing guidelines, whereas physicians must focus on the individual patient's clinical responses.
- It is essential to implement a personalized care framework, in which the patient demographic profile (race, age, frailty, risk factors, associated diseases, and HMOD) and BP will both have an equal effect on the choice and need for antihypertensive medications and the treatment targets.

Nonpharmacological Therapy

Lifestyle measures should be instituted in all patients, including those who require immediate drug treatment. Patients must be educated about the various aspects of the disease and adherence to lifestyle changes such as a healthy diet low in sodium, regular physical activity, limiting alcohol intake, managing stress, quitting smoking, and monitoring BP at home regularly on a long-term basis.[6,34,35]

Precise lifestyle changes include the following:

- *Salt intake*: Epidemiological evidence indicates an association between salt consumption and increased BP. It is recommended that the total daily salt intake be limited to 5 grams, equivalent to approximately 2.3 grams of sodium; however, this restriction may be eased during hot summer months. The consumption of a diet that is high in fruit, vegetables, nuts, and unsaturated oils and low in sodium can lower BP. A variety of foods rich in nutrients such as potassium, calcium, and magnesium that can help lower BP in some individuals should be incorporated. Patients should be advised to avoid added salt, processed foods, and high-sodium foods such as pickles, papads, chips, chutneys,

Table 20: Blood pressure treatment initiation based on BP category and CV risk

BP (mm Hg)	*Optimal/Normal BP (<130/85 mm Hg)*	*High BP (130–139/85–89 mm Hg)*		*Hypertension (<140/<90 mm Hg)*
Risk		All adults with SBP 130–139 mm Hg AND no high-risk conditions or risk factors	SBP 130–139 mm Hg AND high-risk conditions (e.g., established CVD, diabetes mellitus, CKD, FH or HMOD)	Assumed all at sufficiently high risk to benefit from pharmacological treatment
Treatment	Lifestyle measures for prevention Screen BP at every opportunity	Lifestyle measures for treatment: Monitor BP yearly	Lifestyle measures and pharmacological treatment (after a 3-month delay). Monitor BP yearly once treatment control is established	Lifestyle measures and pharmacological treatment (immediate) Monitor BP yearly once treatment control is established
Target (mm Hg)	Maintain BP <120/70	Aim BP 120–129/70–79 mm Hg[a]		

BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; FH, familial hypercholesterolemia; HMOD, hypertension-mediated organ damage; SBP, systolic blood pressure; [a]caution in adults with orthostatic hypotension, moderate-to-severe frailty, limited life expectancy, and older patients (aged ≥85 years)

Table 21: Sodium content of foods common in the indian diet (per 100 grams)

Low	*Moderate*	*Moderately high*	*High*
Amla, Cow pea (Lobiya), Bitter gourd (Karela), Ragi, Bottle gourd (Laukee), Vermicelli (Saviyan), Brinjal (Baingan), Semolina (Sooji), Cabbage, Wheat Lady's finger (Bhindi), Maida, Colocasia (Arbi), Cucumber, Grapes, French beans, Sweet lime, Peas, Papaya, Onion, Potato, Yam (Jimikand), Orange, Sapota (Chikoo), Tomato ripe	Raisins, Carrots, Radish, Black gram (Urad) dal, Green gram (Moth) dal, Red gram (Arhar/ Toor) dal whole, Lentil (Masoor), Bengal (Chana) gram, Banana, Pineapple, Apple, Mutton	Cauliflower, Fenugreek (Methi), Lettuce (Salad Patta), Field beans, Beetroot, Watermelon, Bengal gram, Red gram dal, Tender liver, Prawns, Beef, Chicken	Amaranth (Rajgira), Bacon, Egg, Lobster

Low, <25 mg; moderate, 25–50 mg; moderately high; 50–100 mg; high >100 mg

and preparations containing baking powder. Most breads, cereals, packaged namkeen, readymade soups, canned food, pizzas, and Chinese takeaways are also high in salt content. The salt content of some commonly used food items is given in Table 21.

- In the Indian context, salt restriction is more important as Indian cooking involves a high usage of salt. Salt intake is notably high among Indian patients. A study conducted by an ICMR task force across 13 states recorded an average daily salt consumption of 13.8 grams per individual.[36] According to the SCRIPT study conducted in four regions of India, the region-wise mean daily salt intake across four regions (north–14.1 gm; east–9.8 gm; west–10.1 gm; south–9.4 gm) is widely assorted. These values are much higher than the WHO recommendation of <5 gm per day, which is also our IGH guideline recommendation (Fig. 13).[36]
- Dietary Approaches
  - Diet changes have been proven to reduce hypertension; the Dietary Approaches to Stop Hypertension (DASH) framework recommends the consumption of a diet rich in fruits, green leafy vegetables (broccoli, spinach, kale, mustard greens, collard greens), and whole grains (cracked wheat, oats, millets), and low-fat dairy products, lean meats, fish, and eggs. It also emphasizes the need for low-sodium, low-fat dairy products, limiting saturated and total fats, and avoiding processed food items. Animal proteins, including lean meat, low-fat dairy, eggs, and fish, can be incorporated. This dietary pattern can lower BP by up to 11 mm Hg in patients with high BP.[37]
  - Regular fish consumption may enhance BP reduction in obese individuals.[38]
  - Vegetarians have a lower BP than meat eaters.[39] This is due to the higher intake of fruit, vegetables, whole grains, and fibers.[40]
  - The intake of saturated fats must be reduced since concomitant hyperlipidemia is often present in patients with hypertension.
  - Adequate potassium intake from fresh fruits and vegetables may improve BP control in patients with hypertension. Food items with high potassium levels can be beneficial. The potassium intake should be regulated in CKD patients.
  - Thus, the diet in hypertensive patients should be low in calories, fat, and sodium, accompanied by a normal protein intake. The food items to be avoided in patients with hypertension include added salt, processed foods, and high-sodium foods such as pickles, papads, chips, chutneys, and preparations containing baking powder.[41–43]
- Weight reduction
  - Highlighting the necessity of maintaining a healthy weight is crucial.
  - Each kilogram (approximately 2.2 pounds) of weight loss may lead to a reduction in BP to about 1 mm Hg. Scientific research indicates that a weight reduction of even as little as 4.5 kg has been found to reduce BP in a large proportion of overweight individuals with hypertension.[44] Additionally, some studies report that losing approximately 10 kg may reduce systolic BP (SBP) by 5–20 mm Hg.[45]
  - BMI–Excess abdominal weight can elevate the risk of high BP. Carrying too much weight around the waist can put one at greater risk of high BP.
- Physical activity
  - Regular exercise is linked to various health benefits, including reduced all-cause mortality rates, coronary heart disease, hypertension, stroke, type 2 diabetes mellitus, metabolic syndrome, colon cancer, and depression.[46] A program involving 30–45 minutes of brisk walking or swimming at least 3–4 times a week could lower SBP by 7–8 mm Hg. Recommendations for at least 150 minutes/week of moderate intensity aerobic exercise (≥30 min, 5–7 days/week) can be maintained. Alternatively, 75 min of vigorous-intensity exercise over 3 days per week may be performed. Patients with elevated BP and hypertension may benefit from daily exercise to improve their 24-hour BP profile and avoid BP peaks on sedentary days.
  - Aerobic exercise should be complemented by low- or moderate-intensity resistance training 2–3 times per week. This may include dynamic resistance exercises, starting with 2–3 sets of 10–15 repetitions, or

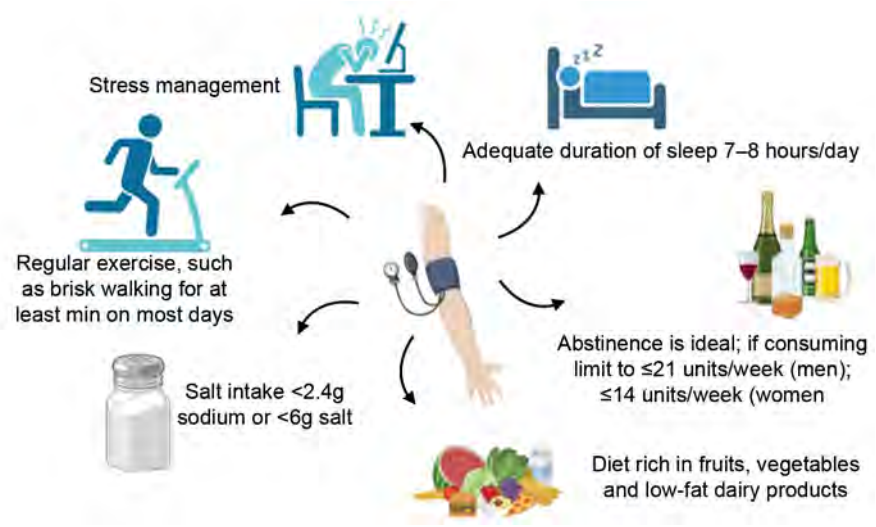


Fig. 13: Nonpharmacological management of hypertension

isometric resistance training involving 3 sets of 1–2 min contractions (such as handgrip, plank, or wall sits).[5] In patients with uncontrolled hypertension at rest, high-intensity exercise should be approached with caution, as a resting systolic BP of >200 mm Hg or a diastolic BP of >110 mm Hg may be a relative contraindication.

- Alcohol intake: It is always advisable to refrain from consuming alcohol as excess alcohol intake causes a rise in BP, induces resistance to antihypertensive therapy, and also increases the risk of stroke.[45,46] Alcohol consumption should be limited to no more than 2 drinks per day (24oz beer, 10 oz wine, 3oz 80-proof whiskey) for most men and no more than 1 drink per day for women and people with lower body weight.[46,47] Studies report that about 50% of heavy drinkers experience a pressor effect and experience a reduction in BP with curtailing their alcohol consumption.[48]
- Smoking: Smoking or the consumption of tobacco in any form is the single most powerful modifiable lifestyle factor for the prevention of major CVD and non-CVDs in patients with hypertension.[49–51] Tobacco consumption leads to an immediate elevation in sympathetic nervous system activity, resulting in an increased demand for myocardial oxygen due to heightened BP, heart rate, and myocardial contractility.[50] The cardiovascular benefits of smoking cessation can be seen within 1 year in all age groups.[51] Although E-cigarettes are now available in India, these are also harmful, and their use must be strongly discouraged.
- Stress management: In hypertensive patients in whom stress may be contributing to BP elevation, stress management should be considered as an intervention.
- Yoga and meditation: Different meditative practices including Tai Chi or yoga which incorporate stretching, meditation, postural control and deep breathing techniques, may help lower stress and autonomic nervous system activity, both of which may contribute to BP reduction.[52] A recent study found an average systolic BP reduction of up to 4 mm Hg following lifestyle modification (LSM) alone, and up to 6 mm Hg when LSM is combined with yoga. Yoga has also been reported to reduce heart rate, waist circumference, and lipid levels, contributing to a reduction in the CVD prevalence and mortality.[53–57]
- Sleep and sleep-related disorders
  - During normal sleep, the BP is typically 10–20% lower than the daytime BP (nocturnal dipping). The absence of nocturnal dipping (non-dipping) is an independent risk factor for CV events.
  - Sleep durations of less than 5 hours/day have been linked with the development of high BP. Conversely, sleeping >9 hours/day has also been linked with high BP.[58]
  - Patients with chronic insomnia have a higher risk of high BP.
  - Obstructive sleep apnea (OSA) and hypertension are closely linked. Approximately 50% of patients with OSA are hypertensive, and an estimated 30% to 40% of patients with hypertension have OSA.
  - A cross-sectional analysis conducted in New Delhi reported that individuals with screen time >390 minutes (6 hours and 30 minutes) had higher odds of elevated BP ($p < 0.05$) with or without correction for high BMI.[59] Longer television screen time has also been shown to been linked with higher systolic BP after adjusting for potential sociodemographic and lifestyle confounders.[60]
  - Taking breaks from screens and limiting exposure to digital stimuli, especially before bedtime, can promote better sleep hygiene which is crucial for BP regulation.[61]
  - Thus, sleep and BP are closely linked. Maintaining a regular sleep routine with adequate duration and good quality of sleep is important for effective BP regulation.
- Caffeine, energy drinks, and sugar-sweetened beverages
  - Caffeine intake increases BP acutely, but there is a rapid development of tolerance to its pressor effect. Epidemiological studies have not demonstrated a direct link between caffeine intake and high BP.[45]
  - Energy drinks with high concentrations of ingredients such as taurine and caffeine increase BP and may lead to acute or chronic CV complications in young adults
  - Sugar-sweetened beverages should be avoided. Consuming more than 2 servings per day has been associated with a 35% higher risk of CVD and with increased all-cause mortality. In children and adolescents, sugar-sweetened beverages increase systolic BP and the risk of incident hypertension.
- Environmental pollution
  - Noise pollution: Studies have reported that environmental noise, particularly from traffic, can be a significant risk factor for hypertension. A meta-analysis of 26 studies conducted by a WHO expert group reported a relative risk (RR) of 1.05 (95% CI, 1.02–1.08 per 10 dB LDEN) for the prevalence of hypertension in response to exposure to road traffic noise.[62] The CASPIAN-V study on non-communicable diseases revealed that higher levels of noise annoyance and psychological distress were associated with increased BP among children and adolescents. The design of cities with an emphasis on heart health is of paramount importance. This involves mitigating heat island effects through the enhancement of green infrastructure and the minimization of built environments.[63]
  - Air pollution: Air pollution is caused by a complex mixture of particulate matter (PM) and gaseous components that can have independent effects on the body, while also potentially exerting synergistic and antagonistic effects. Recent epidemiological research indicates that particulate pollutants significantly increase BP levels, irrespective of whether the exposure is brief or prolonged. PM is classified according to aerodynamic diameter: <10 µm (PM10), <2.5 µm (PM2.5), <0.1 µm (PM0.1) and 2.5 to 10 µm (PM2.5–10). A prospective epidemiological study from urban Delhi, India, involving 5,342 participants, demonstrated strong longitudinal associations using repeated measures between ambient PM 2.5 exposure, BP and incident hypertension. Both short-term and long-term exposure contributed to higher BP and an increased risk of incident hypertension.[64]
- Seasonal variations
  - In individuals undergoing treatment for hypertension, significant seasonal variations in BP, such as a marked decrease during the summer or an increase during winter, may necessitate adjustment to antihypertensive therapy.
  - Healthcare providers need to assess seasonal variations in BP among individual hypertensive patients and identify instances where treatment adjustments may be necessary.[65–67]

Pharmacological Therapy

Principles of Drug Treatment

Over the past decade, the goals of treatment have shifted from only lowering BP to focusing on overall health and preventing HMOD.

The gradual reduction of BP should be achieved. Low doses of antihypertensive drugs should be used to initiate therapy.

Five classes of drugs can be recommended as first-line treatment for stage I and II hypertension.

These include: (1) ACE inhibitors, (2) Angiotensin receptor blockers (ARBs), (3) Calcium channel blockers (CCBs), (4) Diuretics, and (5) Newer β-blockers.

The choice of an antihypertensive agent is influenced by age, concomitant risk factors, presence of HMOD, other co-existing diseases, socioeconomic considerations, drug availability and the experience of the physician.

Combining low doses of two or more drugs with a synergistic effect is likely to produce fewer side effects. In 70% of patients, reduction will be achieved with two or more agents only. Utilizing long-acting drugs that deliver 24-hour efficacy through a single daily dose facilitates the seamless and stable management of BP and improves patient compliance.

Once hypertension is effectively controlled, the possibility of decreasing the dosage and number of antihypertensive medications (step-down therapy) should be evaluated.

Due to a greater seasonal variation of temperatures in India, marginal alterations in drug dosages may be needed from time to time.[66,67]

The commonly used antihypertensive class of agents is discussed below:

- Antihypertensive drugs
  - Angiotensin converting enzyme inhibitors (ACE Inhibitors): ACE Inhibitors are first-line treatments for individuals with diabetes, metabolic risk factors, a history of myocardial infarction, and heart failure. In diabetes mellitus, they slow down renal progression, especially in those with microalbuminuria and early CKD. Moreover, they are metabolically beneficial and help mitigate other risk factors such as dyslipidemia and diabetes.
  - The most common side effect of ACE Inhibitors is a dry cough. ACE inhibitors are contraindicated in pregnancy. Serum creatinine and potassium should be monitored in patients receiving ACE inhibitors. Ramipril and Perindopril have greater tissue ACE inhibition effects than other agents. In particular, Perindopril in combination with Indapamide has been shown to reduce mortality in patients who have survived stroke (PROGRESS trial).[68]
  - Angiotensin receptor blockers: ARBs block the angiotensin II AT-1 receptors and thus prevent the action of angiotensin II. The findings from the LIFE trial indicated that losartan was more effective than atenolol in lowering the incidence of the primary composite endpoint, which includes stroke, myocardial infarction, and CV mortality.[69] In the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial, both valsartan and amlodipine reduced BP in hypertensive patients at high CV risk, but the effects of the amlodipine-based regimen were more pronounced, especially in the early period.[70]
  - Cough and angioedema are much less frequently encountered than with ACE inhibitors.[71] Initially, there were some fears regarding the increase in coronary events following the use of these agents; however, these fears have proven to be unfounded. According to the ONTARGET trial, telmisartan (80 mg daily) is as effective as ramipril (10 mg daily) in lowering CV events in patients who are at a high risk due to vascular disease or diabetes.[71] The use of both ACE inhibitors and ARBs together should be avoided as this may lead to a high risk of hypotension and hyperkalemia. In the randomized double-blind ROADMAP trial involving 4,447 diabetic patients treated with olmesartan (40 mg OD), the onset of microalbuminuria was found to be delayed in those with type 2 diabetes.[72] A recommendation for the careful monitoring of eGFR changes and serum potassium levels should be incorporated. This monitoring should be conducted one week after the initiation of the therapy and after every dosage increment.
- Calcium channel blockers
  - The two subgroups of CCBs are dihydropyridines (amlodipine, felodipine, nifedipine, cilnidipine) and non-dihydropyridines (verapamil and diltiazem). Amlodipine is the most commonly used CCB. CCBs are particularly recommended for elderly patients with isolated systolic hypertension. Verapamil and diltiazem reduce heart rate and have negative inotropic effects. In the Nordil trial,[73,74] treatment based on diltiazem was shown to be as effective as treatment based on diuretics, β-blockers, or both, in preventing the combined primary endpoints of stroke, MI, and CV deaths. The findings of the ASCOT-BPLA (BP Lowering Arm) study show that an antihypertensive drug regimen starting with amlodipine (adding perindopril as required) is better than one starting with atenolol (adding thiazide as required) in terms of reducing the incidence of all types of CV events and all-cause mortality, and risk of subsequent new-onset diabetes.[31]
  - Short-acting dihydropyridines (nifedipine) should be avoided. Amlodipine does not affect heart rate and cardiac contractility and is safe for use in patients with congestive heart failure.[74]
- Diuretics
  - Diuretics are widely used as first-line anti-hypertensive drugs. They are effective and affordable. Although high-dose diuretic therapy has been associated with side effects, currently recommended low-dose diuretic therapy is generally well tolerated. Low-dose diuretics have fewer metabolic side effects such as reduced glycemic control, hyperuricemia, and dyslipidemia. Diuretics should be used in doses equivalent to 12.5 mg daily of chlorthalidone or hydrochlorothiazide to avoid adverse metabolic consequences.
  - Chlorthalidone is preferred over hydrochlorothiazide as an antihypertensive.[75] While indapamide use is associated with minimal metabolic side effects, combinations of thiazides and potassium-sparing diuretics (amiloride and triamterene) are also effective options. Findings from the 2016 PATHWAY 3, a double-blind randomized trial indicated that a combination of amiloride with hydrochlorothiazide prevents glucose intolerance and improves BP regulation compared with hydrochlorothiazide alone. Thus, when hydrochlorothiazide is used as a first-line agent it can be used in combination with amiloride.[76] On the basis of previous evidence, chlorthalidone has emerged as a superior drug compared to hydrochlorothiazide. As an evidence-based preferred diuretic, low-dose chlorthalidone can be used as monotherapy or as part of

combination therapy for effective BP control and target organ protection.

- Aldosterone antagonists, such as Spironolactone and Eplerenone, are the recommended add-on medications for lowering BP in patients experiencing resistant hypertension, even when hyperaldosteronism is not established. The PATHWAY-2 study (2015), a randomized double-blind crossover trial, showed that spironolactone was superior to doxazosin and bisoprolol as an add-on agent among patients with resistant hypertension who were already on a three-drug combination (ACE Inhibitor/ARB + CCB + thiazide diuretic).[77,78] In cases of heart failure and/or renal failure, loop diuretics like Furosemide (40–80 mg) and Torsemide (10–40 mg) may be used. Metolazone (2.5–5 mg) is the only thiazide-like diuretic that is known to be effective in patients with renal failure.

- β -blockers
  - Several head-to-head trials have reported that β-blockers are less effective than ACE inhibitors or CCBs at reducing the risk of diabetes and stroke. This is particularly true in patients taking β-blockers and diuretics. However, in most of the studies, the β-blocker examined was atenolol. In the absence of substantial data on other agents, it would not be appropriate to apply this conclusion to all β-blockers. β-blockers are less effective at reducing central aortic pressure than other classes of antihypertensive agents, which may explain the failure to reduce mortality. They also have limitations in patients with dyslipidemia and impaired glucose tolerance. However, they can be prescribed for younger patients with hypertension, those with stable and unstable angina, patients post-MI with hypertension, and patients with heart failure. Agents with intrinsic sympathomimetic activity and highly selective β-blockers such as bisoprolol and nebivolol have lesser metabolic adverse effects. Labetalol is an α and β blocker and is the drug of choice for hypertension in pregnancy.[78] Racemic forms of calcium channel blockers and β-blockers are presently available. However, long-term studies regarding their efficacy and safety are not available.
- Other drugs
  - α-blockers: Prazosin, terazosin, and doxazosin effectively reduce BP both as monotherapy and in combination with other drugs. They hold a significant role in the management of elderly patients with hypertension, benign prostatic hyperplasia (BPH), and chronic kidney disease (CKD).[1,78,79] Since postural hypotension can occur, the dose of α-blockers should be carefully up-titrated. Data from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) demonstrated that patients in the doxazosin-based arm had a 25% increase in CV events and twice the risk of congestive heart failure.[32] Hence, these agents are not to be used as first, second, or third-line agents but are generally used as an add-on therapy for resistant hypertension.
  - Centrally Acting Drugs: α-Methyldopa, clonidine, and moxonidine have been in use for several years. Methyldopa is an important agent for the treatment of hypertension in pregnancy. Clonidine, though a potent antihypertensive agent, is not used frequently due to side effects such as postural hypotension, anticholinergic effects, and problem of withdrawal-related rebound hypertension. These agents are used in patients with chronic kidney disease (CKD) with resistant hypertension.
  - Direct Vasodilators: Though hydralazine and minoxidil demonstrate efficacy, side effects such as tachycardia, headaches, and the retention of sodium and water may pose challenges in their application for treating hypertension in current medical practice.
  - Angiotensin Receptor–Neprilysin Inhibitor (ARNI): Sacubitril/valsartan is the first ARNI drug available worldwide for heart failure. Sacubitril inhibits neprilysin activity, thereby increasing the body's levels of natriuretic peptides, which then reduce BP and protect organs. While valsartan effectively counteracts activation of the renin-angiotensin-aldosterone system (RAAS), the combination achieves multi-target blood pressure reduction. A total of 14 sacubitril/valsartan trials have shown great results for different types of hypertension, including grade 1 and 2 hypertension, refractory hypertension, hypertension in the elderly, and salt-induced hypertension among others. In the future, this drug may become the standard of care for hypertension.[80]
  - Sodium-glucose transporter-2 (SGLT-2) Inhibitors: Empagliflozin, canagliflozin and dapagliflozin have been evaluated recently amongst diabetic patients in three large trials (EMPA-REG, CANVAS Program and DECLARE-TIMI). These agents have significant CV benefits and reduce BP. Notably, they reduce BP significantly in patients with diabetes or hypertension, irrespective of the level of BP.[81]

The choice of agent among the five classes depends on age, risk factor profile, and associated comorbidities. Tables 22 to 26 present guides to selection of the appropriate antihypertensive drugs including dosages and side effects.

Antihypertensive Drug Combinations

Combination therapy enables the effective control of hypertension since a majority of patients will require two or more drugs for sustained and effective control of BP.[1,5] To attain effective BP control with minimal side effects, it is often essential to integrate several classes of drugs with different mechanisms of action to effectively control BP with minimal side effects. Combinations that provide additive hypotensive effects can produce more significant BP reductions than monotherapy. For stage 1 hypertension or higher, therapy can be initiated either with two drugs or using a fixed-dose combination. The ACCOMPLISH trial has shown that a combination of ACE inhibitors with CCBs is better than a combination of ACE inhibitors with diuretics.[82]

In younger individuals, high-renin hypertension is prevalent, leading to a preference for combinations including ACE inhibitors, ARBs, or the latest beta-blockers. While older individuals have low-renin hypertension, and hence combinations including diuretics or CCBs are preferred as first-line agents. In case the BP is not controlled with initial low dose combination therapy of two agents (step 1), a combination of three drugs case be used (A, B, C or D) (Step 2). In case the BP is not controlled with low-dose triple drug combination therapy, the doses can be escalated to maximally tolerated triple drug combination therapy (step 3). In resistant hypertension patients, when the BP is not controlled inspite of triple drug therapy (one of the drugs should be a diuretic), mineralocorticoid receptor antagonists (MRA) should be added–spironolactone or eplerenone (step 4). The step care approach for physicians suggested by the present IGH V guidelines for combination therapy in hypertension is shown in Figure 14.

- Before making a diagnosis of resistant HTN, rule out secondary causes and pseudo-

Table 22: Guidelines for selecting the most appropriate antihypertensive medications

Class of drugs	*Definite indications*	*Possible indications*	*Definite contraindications*	*Relative contraindications*
Diuretics	Heart failure, elderly patients, systolic hypertension	Diabetes	Gout	Dyslipidemia
Calcium channel blockers (CCBs)	Angina, elderly, systolic hypertension, diabetes, metabolic syndrome	Peripheral vascular disease, CVA	Heart block*	Congestive heart failure*
Angiotensin receptor blockers (ARBs)	Metabolic syndrome, diabetes mellitus, proteinuria, left ventricular dysfunction, heart failure, ACE inhibitor-induced cough	CVA	Pregnancy and lactation, bilateral renal artery stenosis, hyperkalemia, a rise of creatinine by 30% in 4 weeks	Moderate renal failure (creatinine >3 mg/dL, eGFR <15 mL/min/ 1.73 m^2)
Angiotensin-converting enzyme inhibitors (ACEIs)	Metabolic syndrome, proteinuria, diabetes mellitus, LV dysfunction, heart failure, post-myocardial infarction	CVA	Pregnancy and lactation, bilateral renal artery stenosis, hyperkalemia, a rise of creatinine by 30% in 4 weeks	Moderate renal failure (creatinine >3 mg/dL, eGFR <15 mL/min/ 1.73 m^2)
β-blockers	Angina, postmyocardial infarction, tachyarrhythmia, heart failure	Pregnancy, diabetes	Heart block	Dyslipidemia, peripheral vascular disease, asthma, and chronic pulmonary diseases, elderly person >50 years, regular physical activity

[a]Verapamil or diltiazem; ACE, angiotensin-converting enzyme; CVA, cerebral vascular accident; ARBs, angiotensin receptor blockers; CCBs, calcium channel blockers

Table 23: Special circumstances for add-on therapy after first-line antihypertensive drugs

Class of drugs	*Definite indication*	*Possible indication*	*Definite contraindication*
α-blockers (doxazosin, prazosin)	Prostatic hypertrophy, CKD, resistant hypertension	Glucose intolerance, dyslipidemia	Orthostatic hypotension, congestive heart failure
Centrally acting agents (α-methyldopa, clonidine)	Hypertension in pregnancy, resistant hypertension	CKD	Acute or chronic liver disease, pregnancy, lactation
Vasodilators (hydralazine)	Resistant hypertension, hypertension in pregnancy		Coronary artery disease
Angiotensin receptor-neprilysin inhibitor (sacubitril valsartan)	Metabolic syndrome, diabetes mellitus, proteinuria, left ventricular dysfunction, heart failure, ACE inhibitor-induced cough	CVA	Pregnancy, lactation, bilateral renal artery stenosis, hyperkalemia, rise of creatinine by 30% in 4 weeks

CVA, cerebral vascular accident; CKD, chronic kidney disease

resistance; Prescribe self-blood pressure monitoring for all those patients who can afford it.

- Add newer β-Blockers at any stage in case of angina, post-MI, HF, or for heart rate control.
- Lifestyle changes must be an integral part of BP management.

Certain drug combinations have synergistic effects and increase the effectiveness of the other agent. However, some combinations are not effective and are thus undesirable and not recommended, as presented in Table 26.

Maintenance and Follow-up Therapy

Once therapy with a particular set of antihypertensive drugs is initiated, patients need to be monitored at frequent intervals during stabilization to observe changes in BP and see whether non-drug measures are being strictly followed. At least once a fortnight, BP should be measured at the clinic or at home. Other CHD risk factors and co-existing diseases/conditions should be monitored. The overall risk category of a patient and the level of BP decide the frequency of follow-up visits to a large extent. The frequency can be reduced once BP is stabilized and other risk factors are controlled. Tobacco avoidance and alcohol moderation must be promoted vigorously.

The use of single-pill combination (SPC) antihypertensive medications has been shown to improve BP regulation and increase adherence to prescribed treatments among patients with hypertension. However, it is still unclear how effectively these commercially available SPC options can be utilized to achieve a stringent systolic BP goal of under 130 mm Hg. An analysis of 3833 SPRINT participants found 40.3% used regimens available as SPCs, with 3.2% of all regimens matching SPC class-equivalent products. Notably, no SPCs exist for regimens with ≥4 medication classes, which were used by 27.7% of participants. Thus, expanding SPC availability could enhance treatment adherence and outcomes in real-world settings.[83]

Adherence

Medical adherence is effective in managing hypertension. Poor adherence defined as the inconsistent or incorrect use of prescribed antihypertensive medications, can lead to uncontrolled BP and increased CV risk. Factors affecting adherence include patient-physician communication, side effects, treatment complexity, and access to medication.[84] Self-monitoring of BP has been shown to increase adherence. SPCs improve the adherence to BP treatment, and their use is associated with lower all-cause mortality.[85]

Associated Therapies

To reduce the overall risk, patients with hypertension need therapies for controlling additional modifiable risk factors not

Table 24: Commonly Used Dosages and Agents in Each Antihypertensive Drug Class

Class	*Drug*	*Dosage (mg/day)*	*Dosing (frequency/day)*
Diuretics	Hydrochlorothiazide	6.25–12.5	1–2
	Chlorthalidone	6.25–12.5	1
	Indapamide	1.5–2.5	1
	Amiloride	5–10	1–2
	Triamterene	50–100	1–2
	Spironolactone	25–50	1–2
	Eplerenone	25–50	1–2
β-blockers	Metoprolol	25–100	1–2
	Bisoprolol	2.5–10	1
	Nebivolol	2.5–5	1
α + β Blocker	Carvedilol	3.125–50	2
	Labetalol	50–200	2
CCBs	Amlodipine	2.5–20	1
	Cilnidipine	5–10	1
	Diltiazem	90–360	1–2
	Nifedipine (Long acting)	10–120	1
	Verapamil	80–240	1–2
	Benidipine	4–8	1
	Efonidipine	20–40	1
	Azelnidipine	8–16	1
Racemic isomers	S-amlodipine	2.5–10	1
ACE inhibitors	Enalapril	2.5–20	1–2
	Lisinopril	2.5–20	1
	Ramipril	1.25–10	1
	Perindopril	2–8	1
ARBs	Losartan	50–100	1–2
	Candesartan	8–32	1–2
	Valsartan	40–320 ma	1
	Irbesartan	150–300	1
	Telmisartan	20–160	1
	Olmesartan	20–40	1
	Azilsartan	80	1
	Fimasartan	60–120	1
α-blockers	Prazosin	2.5–10	2–3
	Doxazosin	1–4	1
Centrally acting drugs	Clonidine	0.1–0.3	2
	Methyldopa	500–1500	2
	Moxonidine	0.2–0.4	1–2
Vasodilators	Hydralazine	25–100	2
	Minoxidil	2.5–5	1–2
ARNI	Sacubitril valsartan	50–200	2

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor; CCBs, calcium channel blockers; ARNI, angiotensin receptor–neprilysin inhibitor

only for secondary prevention but, as indicated by recent evidence, also for primary prevention. Low-dose aspirin should be prescribed to all hypertensive patients with CVD and stroke (secondary prevention). All hypertensive patients with coronary, peripheral, or cerebrovascular disease and LDL levels >100 mg/dL should receive statins as a secondary prevention strategy. Hypertensive patients without CVDs but who are in high-risk groups should also receive statins for primary prevention, as shown in the recently published HOPE III trial. Rosuvastatin 10 mg/day resulted in greater benefits than even antihypertensive drugs in a high-risk hypertensive population.[86–88] Aspirin has no role as a concomitant therapy in patients with hypertension without evidence of ASCVD. Recently, three primary prevention trials–the ASCEND, ARRIVE, and the ASPREE trials looked at the role of aspirin for primary prevention in elderly (ARRIVE and ASPREE) and diabetic (ASCEND) individuals. All three trials revealed no benefit of aspirin as a primary preventive agent.[89–91]

Therapeutic inertia refers to the reluctance of healthcare professionals to either commence or escalate treatment in accordance with established guidelines. Reasons for therapeutic inertia may include time constraints, lack of awareness of current guidelines, overconfidence in current treatment, or inadequately BP monitoring. Continuous education on best practices for managing hypertension is essential for healthcare providers, particularly to recognize and address the challenges posed by therapeutic inertia.[92]

Adverse Drug-to-drug Interactions

Adverse drug-to-drug interactions occur when the primary mechanism of action of one class of medication (e.g., bradycardia with a beta blocker) is excessively intensified by the concurrent use of another antihypertensive agent (e.g., verapamil). Sometimes, the normal actions of one drug become amplified, causing a side effect. In other instances, interactions manifest at the molecular level when the same liver enzyme metabolizes drugs like with amlodipine and simvastatin.[93] Table 27 presents an overview of significant drug interactions associated with each class of antihypertensive medications.

Adverse Events

Considering the significant diversity among patients, the ideal pharmacological management of hypertension requires a flexible approach. This approach should involve the use of the lowest effective initial dose to establish a positive therapeutic relationship and to reduce adverse drug events that may affect patient compliance. Low-dose therapy provides a period where patients can psychologically adapt to their hypertension diagnosis and to begin implementing the lifestyle changes prescribed by their doctor. For most patients, therapy should commence with a minimal dosage to avoid the potential adverse effects that may arise from a drastic or rapid reduction in BP.[94]

First-dose Reactions

First-dose reactions are adverse drug events that occur with the initial dose of a drug or when the dosage is increased. First-dose reactions have been reported with α-receptor blockers, CCBs, ACE inhibitors,

Table 25: Side effects associated with common antihypertensive drugs

Common side effects	*ACE inhibitor*	*ARB*	*CCB*	*Diuretic*	*β-blocker*
Headache	–	–	+	–	–
Flushing	–	–	+	–	–
Lethargy	–	–	–	–	+
Impotence	–	–	–	+	+
Dry cough	+	±	–	–	–
Gout	–	–	–	+	–
Edema	–	–	+	–	–
Postural hypotension	+	+	–	+	–
Cold hands and feet	–	–	–	–	+
Hyperkalemia	+	+	–	–	–
Hyperglycemia	–	–	–	+	+
Dyslipidemia	–	–	–	+	+
Angioedema	+	+	–	–	–

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor; CCB, calcium channel blocker

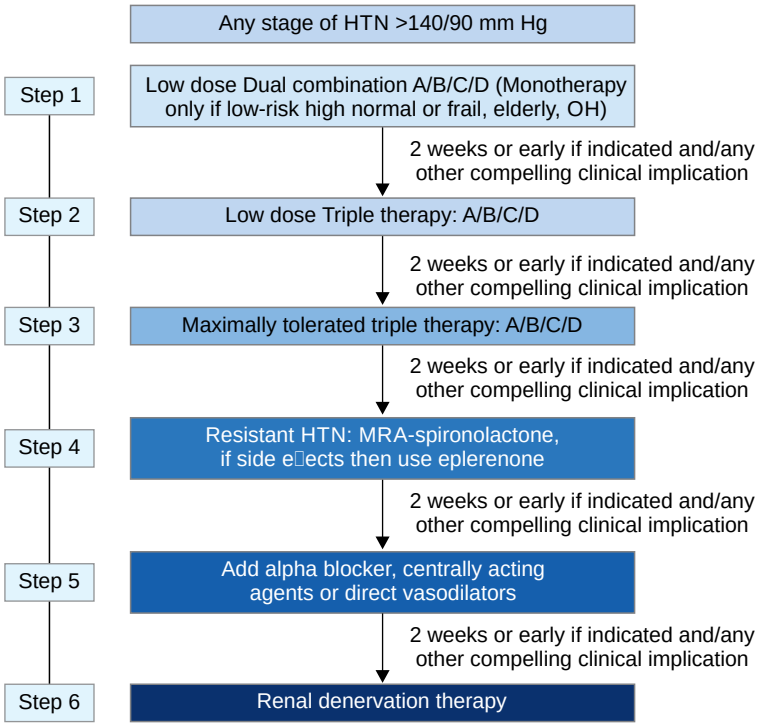


Fig. 14: Step-care approach for combination therapy in hypertension according to the IGH V Guidelines

and β-blockers, but clinical experience suggests that first-dose reactions can occur with any antihypertensive drug. The reactions observed after the first dose of antihypertensive treatments are typically dose-related and may result from a rapid decrease in blood pressure. This can lead to symptoms such as postural hypotension, dizziness, syncope, headaches, lethargy, and other related effects.[94] BP-lowering medications have multiple side effects, which may be more common in females. Although these medications are generally well tolerated, their common side effects include headaches, cough, postural hypotension, syncope, lethargy, dizziness or light-headedness, diarrhea or constipation, fatigue, ankle edema, and erectile problems, depending on the drug class.[95–97]

Initial Doses for Older Patients

Hypertension is most common in patients over 60 years of age, and its management is challenging due to altered pharmacokinetics such as reduced liver and kidney function, and high receptor sensitivity resulting in a greater variability of drug responses. In geriatric patients, the probability is highly intensified as two-thirds of people take at least one medication daily, with an average of three prescription and/or non-prescription drugs. Hence, adverse effects are two to three-fold more frequent in older patients than other populations and are typically dose-related.[96]

Among the various therapeutic medications, diuretics are known to disrupt electrolyte balance, leading to issues such as hypokalemia, hypomagnesemia, and hyponatremia. ACE inhibitors may induce hyperkalemia, whereas, diuretics and nonselective beta-blockers, particularly those without intrinsic sympathomimetic activity, have been linked to disturbances in glucose and insulin metabolism, causing adverse changes in circulating plasma lipid profiles. Hyperuricemia linked to diuretic use appears to be a concern primarily for patients who are predisposed to elevated uric acid levels.[98]

Older patients with hypertension, who are fit and capable of independently performing daily activities, will benefit from guideline-directed treatment similar to younger patients, irrespective of their chronological age.[99] However, it is important to customize treatment goals and plans for frail older patients to prevent unintended consequences. This should include assessing frailty, including cognitive status, risk of falls, the propensity for symptomatic orthostatic hypotension, polypharmacy, and other comorbid conditions.[100,101]

Table 26: Undesirable combinations

β-blocker and centrally acting drugs
β-blocker and verapamil/diltiazem
ACE inhibitors and ARBs
Two drugs from the same class

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor

Antihypertensive Drug Combinations

Combination therapy is the preferred method for effective control of hypertension since a majority of patients will require two or more drugs for sustained and effective control of BP.[1,5]

One often needs to combine different classes of drugs with different mechanisms of action to achieve effective BP control with minimal side effects. Combinations with additive hypotensive effects will produce greater BP reductions than those obtained with monotherapy. When a subject is in stage 1 hypertension or above, therapy can be initiated either with a low dose of two drugs or as a fixed-dose combination. The ACCOMPLISH trial has shown that a

combination of ACEIs with CCBs is better than a combination of ACEI with a diuretic and should be the preferred combination.[82] In refractory patients, when three agents are to be used, A+C+D is a good choice. This must be titrated to the maximal tolerated dose.[71]

Certain drug combinations have a synergistic effect and increase the effectiveness of the other agent. However, some combinations are not effective and are thus undesirable and not suggested to be used. These are shown in Table 28.

Drug Interactions of Antihypertensive Drugs by Drug Class

Since multiple drugs are used in hypertensive patients and often these patients have other coexisting conditions, certain common drug interactions should be kept in mind, as shown in Table 28.[102] The sequence of drug therapy after choosing an initial agent depends on the response to the first agent.

Interventions for Hypertension Management: Renal Denervation and Device-based Strategies

Despite various pharmacological and lifestyle interventions, a significant portion of individuals with hypertension still struggle to achieve optimal BP control. Device-based therapies, particularly renal denervation (RDN), have emerged as promising alternatives, especially for those with resistant hypertension.

Table 27: Drug interactions

Drug class	*Interaction*
ACE inhibitors and diuretics	NSAIDs, including COX-2 inhibitors, decrease the efficacy of diuretics and ACE inhibitors
Calcium channel blockers	Verapamil increases the serum levels of several statins, such as atorvastatin, simvastatin, and lovastatin
	Cyclosporin levels are increased with diltiazem and verapamil
Diuretics	Steroids can worsen diuretic-induced hypokalemia and reduce their effectiveness
	Class 1A (quinidine or procainamide) or Class III (sotalol, amiodarone) Antiarrhythmics can prolong the QT interval and may precipitate torsade de pointes in the presence of diuretic-induced hypokalemia
	Combined use of ACE inhibitors or ARBs and potassium-sparing diuretics may result in hyperkalemia
β Blockers	Metoprolol and carvedilol metabolism is inhibited by paroxetine (a selective serotonin reuptake inhibitor–antidepressant), resulting in increased antihypertensive effects
	Concomitant use of non-dihydropyridine CCBs with β-blockers can result in heart blocks.
α-Methyldopa	Concomitant use of tricyclic antidepressants with methyldopa is to be avoided.

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor; CCBs, calcium channel blockers; ARNI, angiotensin receptor–neprilysin inhibitor; NSAIDS, nonsteroidal anti-inflammatory drugs

The Case for Device-based Interventions

While pharmacological treatments are generally effective, they are often associated with challenges such as patient nonadherence, adverse drug reactions, and inadequate responses in specific groups. In this context, device-based interventions present a novel method for addressing the underlying pathophysiological mechanisms of hypertension, particularly the overactivation of the sympathetic nervous system. These approaches aim to complement traditional treatment methods, filling the gaps in current management strategies.[103,104]

Renal Denervation Therapy

- Mechanism of action: RDN specifically targets the renal sympathetic nerves that are crucial for regulating BP. Overactivity of the sympathetic nervous system is responsible for several deleterious effects, including:
- Increased renin release: promoting sodium retention and fluid overload.
- Enhanced sodium reabsorption: leading to increased plasma volume.
- Elevated renal vascular resistance: compromising renal perfusion and function.
- In RDN, the sympathetic nerves are ablated through various methods such as:
  - Radiofrequency ablation where a catheter is used to create thermal lesions.
  - Chemical ablation where neurolytic agents are administered to interrupt sympathetic pathways.
- Ultrasound ablation where focused ultrasound waves are used for precise nerve disruption.

These techniques lead to a sustained reduction in sympathetic activity,

Table 28: Drug Interactions of antihypertensive drugs by drug class

Drug class	*Drug interactions*
β-blockers	Risk of bradycardia. Metoprolol, carvedilol (metabolized via CYP2D6), labetalol, and propranolol may involve hepatic metabolism. Bisoprolol and nebivolol are cleared by both the liver and kidneys, reducing hepatic interaction risks. Atenolol, nadolol, and sotalol lack hepatic metabolism involvement
Calcium channel blockers	Potential for bradycardia and heart block, particularly when combined with rate-lowering agents (e.g., verapamil, diltiazem). Amlodipine and nifedipine may interact with hepatic enzymes when co-administered with simvastatin or atorvastatin
Diuretics	May cause hypokalemia, which can be mitigated by the simultaneous use of ACE inhibitors or ARBs. Hyponatremia should also be evaluated from time to time
ACE inhibitors, ARBs, and renin inhibitors	Hyperkalemia can occur, which may be counteracted by concurrent diuretic use
Aldosterone blockers	When used with spironolactone or eplerenone in hypertensive heart failure, there is an increased risk of hyperkalemia
α-blockers	Fluid retention, especially in heart failure, can be managed by adding diuretics

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor

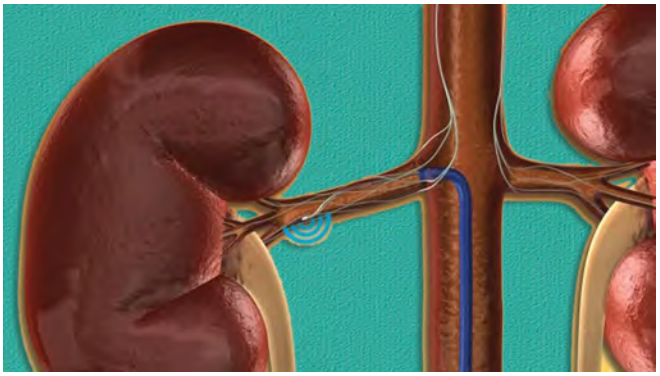


Fig. 15: The Medtronic Symplicity Catheter

promoting consistent BP-lowering effects that are less dependent on medication adherence (Adapted from: https://www.dicardiology.com/article/development-renal-denervation-therapy).[104]

Clinical Evidence

- The effectiveness and safety of RDN have been demonstrated through numerous high-quality randomized controlled trials.
- SPYRAL HTN-OFF MED (Pilot and Pivotal Trials): These pivotal studies revealed a 4.7–5.5 mm Hg decrease in 24-hour systolic BP in patients not taking antihypertensive medications, compared to sham controls, after RDN. The findings emphasized the "always-on" effect of RDN, regardless of medication variability.[105]
- RADIANCE-HTN SOLO and TRIO: These trials, which utilized ultrasound-based RDN, reported night-time ambulatory BP decreases of 8.5 mm Hg and 8.0 mm Hg, respectively, in different populations of patients with hypertension.[106,107]
- Global SYMPLICITY Registry: This extensive registry provided real-world data reflecting sustained BP reductions over three years following RDN, with a highly favorable safety profile.[108]
- SPYRAL HTN-ON MED: This study, which involved participants who were prescribed 1–3 antihypertensive medications, demonstrated a marked reduction in ambulatory BP, reinforcing the significance of RDN as a valuable addition to pharmacotherapy.[109]
- Overall, the evidence points to the effectiveness of RDN and other device-based strategies as essential components in managing resistant/difficult-to-treat hypertension.

Patient Selection and Indications

Patient selection is critical to the success of RDN. Current guidelines recommend RDN for:

- Resistant Hypertension: Patients with uncontrolled BP (≥140/≥90 mm Hg) despite the use of ≥3 antihypertensive agents, including a diuretic, at optimal doses.
- Medication intolerance or Non-adherence: Patients unable to tolerate antihypertensive drugs due to side effects or unwilling to adhere to long-term pharmacological regimens.
- Sympathetic Overactivation Syndromes: Patients with conditions such as metabolic syndrome or obstructive sleep apnea, where heightened sympathetic activity contributes to refractory hypertension.

However, clinicians should stay vigilant during patient selection to exclude patients with severe CKD (eGFR <30–45 mL/min/1.73 m^2), renal artery stenosis, anatomical anomalies, and secondary hypertension due to endocrine or renovascular causes. Thus, exhaustive investigations are required to rule out secondary endocrine-renal cases during patient selection.[105]

Place in the Management Algorithm

RDN should be considered as an adjunctive treatment option within the management algorithm for hypertension when target BP is not achieved despite optimal pharmacological therapy and lifestyle modifications. This procedure appears to be particularly beneficial for patients with resistant hypertension who remain uncontrolled despite the use of three or more antihypertensive agents, including a diuretic, at the maximum tolerated doses. For patients who are intolerant to medications or nonadherent due to drug side effects, RDN can serve as a viable alternative. The procedure should be incorporated into a comprehensive treatment plan that includes ongoing lifestyle interventions and regular follow-ups to monitor efficacy and safety (Fig. 15).

Procedural risks: Complication rates are less than 1% and mainly involving issues at the access site or vascular injury, which are managed with proper procedural precautions.

Renal function: Long-term data show no significant decline in renal function or increased risk of renal artery stenosis.

Durability: Significant BP reductions have been sustained for over 3 years, with minimal evidence of reinnervation in treated patients.[110]

Limitations and Areas for Further Research

While RDN shows promise, several questions remain,

- Heterogeneity in response: Not all patients experience significant BP reductions, highlighting the need for predictive biomarkers to stratify patients better.
- Long-term efficacy: Data extending beyond three years are required to confirm the durability of the treatment.
- Integration with pharmacotherapy: Further investigation is needed to optimize the combination of RDN with antihypertensive medications.

Other Device-Based Interventions

Baroreflex Activation Therapy (BAT)

BAT targets the baroreceptors in the carotid sinus, stimulating parasympathetic activity to counteract sympathetic overdrive. This approach has shown promise in reducing BP among patients with resistant hypertension and improving autonomic balance.[111]

Central Arteriovenous Anastomosis

In this intervention, a controlled arteriovenous fistula is generated. The fistula reduces systemic vascular resistance and cardiac afterload. Preliminary studies suggest moderate BP-lowering effects, but long-term data are still pending.[112]

Alcohol-based Chemical Ablation

This method uses dehydrated alcohol delivered via specialized catheters to disrupt renal sympathetic nerves. Initial trials have demonstrated efficacy, but safety concerns and procedural challenges limit its widespread adoption.[113]

Future Directions in Device-based Therapy

- Personalized medicine: Leveraging genetic and biomarker data to identify patients most likely to benefit from device-based interventions.
- Hybrid approaches: Combining RDN with BAT or pharmacological agents for synergistic effects.
- Technology enhancements: Refining catheter designs and energy-delivery systems to improve precision and minimize risk.

Secondary Hypertension

Introduction

SH is a subset of hypertension with an identifiable and potentially correctable cause. SH cases account for approximately 5–10% of all hypertensive cases. Despite its lower prevalence compared to primary hypertension, secondary hypertension carries a disproportionately high risk of severe complications, including hypertensive crises, stroke, aortic dissection, and cardiac events such as MI, arrhythmias and heart failure.[114–116] SH often affects younger patients or those with resistant or refractory hypertension, making its timely diagnosis and management critical.

While primary hypertension is multifactorial, SH arises from specific conditions, such as primary aldosteronism, renovascular disease, CKD, OSA, and drug- or alcohol-induced hypertension. Rarer causes include pheochromocytoma, Cushing's syndrome, thyroid dysfunctions, coarctation of the aorta, and hyperparathyroidism.[117] Early identification of these underlying causes can significantly improve BP control, reduce CV risk, and enhance patient outcomes. Recognizing the clinical importance of SH, international guidelines recommend screening in specific populations: those with early-onset hypertension, resistant hypertension, sudden worsening of BP control, or clinical signs pointing to a secondary cause.[17]

Prevalence of Secondary Hypertension

Secondary hypertension, though less common than primary hypertension, is a significant cause of elevated BP, with identifiable underlying causes that can often be treated or managed to reduce the burden of hypertension-related morbidity. Recent studies suggest that SH accounts for approximately 5% to 10% of all cases of hypertension in the general population.[4,118] However, its prevalence may be higher in specific subgroups, such as younger patients, those with resistant hypertension, and those with a sudden onset of hypertension.[118]

SH is also more prevalent in individuals with certain risk factors or comorbidities. OSA, a condition increasingly recognized as a significant contributor to SH, has been associated with higher BP levels and is found in approximately 60% to 90% of patients with resistant hypertension.[119,120] Moreover, the prevalence of SH increases with age, with a higher frequency observed in those over 60 years old, particularly in relation to renovascular disease and primary aldosteronism.[121]

Although SH remains a less frequent cause of hypertension overall, its early identification is crucial, as successful treatment or management of the underlying cause can often lead to the normalization of BP and a reduction in CV risk.

Etiology of Secondary Hypertension

Secondary hypertension (SH) arises from identifiable, treatable underlying causes, and understanding these causes is crucial for appropriate management. Several conditions and factors contribute to the development of SH, including:

- *Renal causes:* Renovascular disease and CKD are common causes of SH. Renovascular disease, including fibromuscular dysplasia and renal artery stenosis, can lead to hypertension through activation of the renin-angiotensin-aldosterone system (RAAS). In CKD, reduced kidney function leads to fluid retention and increased systemic vascular resistance, contributing to elevated BP.[121]. Rarer causes include Liddle's syndrome, reninoma, polyarteritis nodosa, etc.
- *Endocrine disorders:* Several hormonal imbalances can result in SH:
  - *Primary aldosteronism*: Excess aldosterone secretion leads to sodium retention, potassium loss, and volume expansion, which increase BP.[122]
  - *Pheochromocytoma and paraganglioma*: These catecholamine-secreting tumors lead to episodic or sustained hypertension due to excess norepinephrine and epinephrine.[123]
  - *Cushing's syndrome*: Overproduction of cortisol increases sodium retention, leading to volume expansion and increased BP.[124]
  - *Thyroid disorders*: Both hyperthyroidism and hypothyroidism can cause SH. Hyperthyroidism increases heart rate and cardiac output, while hypothyroidism leads to increased peripheral vascular resistance.[125]
  - *Hyperparathyroidism*: Overproduction of parathyroid hormone leads to increased calcium levels, which can elevate BP.[126]
- *Obstructive sleep apnea*: OSA is increasingly recognized as a significant cause of SH, particularly in patients with resistant hypertension. The intermittent hypoxia and sympathetic activation associated with OSA contribute to increased BP.[127]
- *Drug-induced hypertension*: Certain medications and substances can cause SH, including NSAIDs, corticosteroids, oral contraceptives, and sympathomimetic agents.[128]
- *Other causes*: These include coarctation of the aorta, which causes increased pressure in the upper body, and pregnancy-related hypertension, including preeclampsia.[129,130,131]

When to Suspect Secondary Hypertension[123,132]

Young age of onset < 30 years of age, particularly in the absence of a family history of hypertension:

- Severe hypertension >180/110 mm Hg with onset at age < 20 years or > 50 years.
- Difficult-to-treat or resistant hypertension with significant end-organ damage features.
- Polyuria, low eGFR, nocturia, proteinuria, or hematuria–indicative of renal diseases.
- Absence of peripheral pulses, brachiofemoral delay, and abdominal or peripheral vessel bruits
- History of polycystic kidney disease or palpable enlarged kidneys.
- Symptoms suggestive of endocrine disorders such as muscle weakness, polyuria, polydipsia, weight gain, or abnormal physical findings (e.g., moon facies, buffalo hump in Cushing's syndrome).[132]
- Combination of pain (headache), palpitation, pallor and perspiration–the 4P's of phaeochromocytoma.
- Significant elevation of plasma creatinine with the use of ACE inhibitors/ARBs.
- Family history of polycystic kidney disease, endocrine tumors, or aortic coarctation.
- Hypertension in children.
- History of snoring, daytime somnolence, obesity, short and thick neck indicative of OSA.

Disease Phenotypes related to Secondary Hypertension

Renovascular Hypertension[133,134]

Pathophysiology: Renovascular hypertension is caused by the narrowing or blockage of the renal arteries, leading to reduced renal perfusion. This stimulates the RAAS, resulting in increased sodium retention, vasoconstriction, and elevated BP. The primary causes are atherosclerosis (especially in older adults) and fibromuscular dysplasia (more common in younger patients). Rare causes include embolic events, tumors, thrombi, and extrinsic reasons. Takayasu's disease is

a nonspecific type of panarteritis affecting predominantly young women. Hypertension is mainly due to renal artery stenosis, which can be unilateral or bilateral.

Clinical Presentation: Patients often present with resistant hypertension, a sudden onset of high BP, or an unexplained deterioration in kidney function. There may also be a history of vascular disease or abdominal bruit. Worsening renal function after starting ACE inhibitors/ARBs should raise the suspicion of bilateral renal artery stenosis.

Diagnosis: Imaging studies such as Doppler ultrasonography, CT angiography, or magnetic resonance angiography (MRA) are used to visualize renal artery stenosis. MRI angiography has higher sensitivity (90%) and specificity (92%). Measurement of plasma renin activity (PRA) can also support the diagnosis, with elevated renin levels suggesting renovascular hypertension. 99Tc–DTPA and 123I–Hippuran scans are useful noninvasive investigations that determine the functional status of CKD. Conventional angiography, though invasive, is the gold standard. Intra-arterial injection with digital subtraction angiography (DSA) may be used. However, renal angioplasty with stenting has shown similar outcomes as medical therapy.

Treatment of renal artery stenosis: The treatment goals are the control of BP and the preservation of renal function. In general, there are three options:

- Medical therapy: Percutaneous transluminal renal angioplasty
- Surgery: Patients with fibromuscular dysplasia benefit from percutaneous transluminal renal angioplasty without stenting or surgical revascularization. RAS blockers are the drugs of choice but require monitoring of renal function, especially in cases of significant bilateral renal artery stenosis or unilateral stenosis in a single functioning kidney.

Patients with atherosclerotic renovascular disease do not demonstrate any significant benefit from renal artery intervention, but medical therapy is equally effective in these patients, as shown in the ASTRAL study published in 2009 and the CORAL study in 2014. Renal artery stenting does not confer any benefit in preventing clinical events when added to medical therapy in patients with renal artery stenosis and hypertension or CKD. Renal artery angioplasty and stenting may be considered in patients with hemodynamically significant, atherosclerotic, renal artery stenosis (stenosis of 70–99%, or 50–69% with post-stenotic dilatation and/or significant trans-stenotic pressure gradient), accompanied by:

- Recurrent heart failure, unstable angina, or sudden onset of flash pulmonary edema despite maximally tolerated medical therapy.
- Resistant hypertension.
- Hypertension with an unexplained, unilaterally small kidney or CKD.
- Bilateral renal artery stenosis or unilateral renal artery stenosis in a solitary functioning kidney.

Primary Hyperaldosteronism (Conn's Syndrome)[135]

Pathophysiology: Primary hyperaldosteronism is characterized by the excess production of aldosterone, typically due to an adrenal adenoma or bilateral adrenal hyperplasia. Excess aldosterone leads to sodium retention, potassium excretion, and water retention, resulting in volume expansion and elevated BP.

Clinical presentation: The classic features include hypertension, hypokalemia, and metabolic alkalosis. Many patients present with resistant hypertension, and muscle weakness and fatigue may be noted.

Diagnosis: Screening includes measuring the plasma aldosterone concentration and plasma renin activity (PRA). A high aldosterone-to-renin ratio is highly suggestive. Confirmatory testing involves a saline infusion test, fludrocortisone suppression test, or CT/MRI to assess adrenal pathology.[122]

Treatment: Aldosterone antagonists such as spironolactone or eplerenone are the first-line therapy. If an adrenal adenoma is identified, surgical adrenalectomy may be curative.[135]

Pheochromocytoma[136]

Pathophysiology: Pheochromocytomas are catecholamine-secreting tumors of the adrenal medulla, resulting in the excess production of norepinephrine and epinephrine. This causes episodic or sustained hypertension, with sudden surges in BP, sweating, palpitations, and headaches.

Clinical presentation: Classic symptoms include paroxysmal hypertension, headaches, palpitations, sweating, and tremors. (the combination of pain (headache), palpitation, pallor, and perspiration–4 P's of phaeochromocytoma). Symptoms are often episodic and can be triggered by physical activity, stress, or certain medications.

Diagnosis: Diagnosis is confirmed by measuring 24-hour urinary catecholamines, metanephrines, or vanillyl-mandelic acid (VMA) and plasma metanephrines or normetanephrines. The following drugs should be withdrawn for 48 hours before doing these tests: α-methyldopa, β-blockers, clonidine, and penicillin. Certain vegetables should also be avoided during this period. Patients can be continued on CCBs and ACE inhibitors during evaluation. CT or MRI imaging helps localize the tumor. MIBG scanning is the most specific way of diagnosing adrenal and extra-adrenal pheochromocytomas. Other modalities include PET scan using 18F-fluorodeoxyglucose.

Treatment: The treatment of choice is surgical resection of the tumor. Preoperative management includes alpha-adrenergic blockers (e.g., phenoxybenzamine) to control blood pressure, followed by beta-blockers if necessary to control heart rate. Adrenergic crisis causes hypertensive emergencies and should be treated with an intravenous alpha-1-blocker such as phentolamine, doxazosin, or terazosin, or with intravenous labetalol.[136]

Cushing's Syndrome

Pathophysiology: Cushing's syndrome results from excess cortisol production, either from an adrenal tumor, pituitary adenoma (Cushing's disease), or ectopic adrenocorticotropic hormone (ACTH) secretion. Cortisol increases sodium and water retention, enhances vascular tone, and contributes to hypertension.[132,137]

Clinical presentation: Characteristic features include central obesity, moon facies, buffalo hump, striae, and easy bruising. Hypertension is often present alongside hyperglycemia and osteoporosis.

Diagnosis: The 24-hour urinary free cortisol test is used for screening. The low-dose dexamethasone suppression test and late-night salivary cortisol levels can confirm the diagnosis. ACTH levels help distinguish between pituitary and adrenal causes.

Treatment: Surgical resection of the tumor is the mainstay of treatment. If surgery is not possible, medical management with ketoconazole or mifepristone can be used to control cortisol production.[132]

Thyroid and Parathyroid Disorders

Thyroid disorders: Both hyperthyroidism (excess thyroid hormone) and hypothyroidism (deficiency of thyroid hormone) can cause secondary hypertension[125]

- *Hyperthyroidism* increases cardiac output and heart rate and may also lead to increased peripheral vascular resistance.
- *Hypothyroidism* increases systemic vascular resistance and can lead to diastolic hypertension.

Parathyroid disorders: Hyperparathyroidism, characterized by excess parathyroid hormone (PTH), leads to hypercalcemia, which can increase vascular tone and cause hypertension.

Diagnosis: Thyroid function tests (TSH, T3, T4) and parathyroid hormone levels, along with calcium levels, are crucial for diagnosis.

Treatment: Treating the underlying thyroid or parathyroid disorder typically normalizes BP. This may include thyroid hormone replacement for hypothyroidism or surgical resection of parathyroid adenomas for hyperparathyroidism.[126]

Obstructive Sleep Apnea[127]

Pathophysiology: OSA is characterized by repeated episodes of upper airway obstruction during sleep, leading to intermittent hypoxia, increased sympathetic activity, and elevated BP. Over time, these episodes contribute to sustained hypertension.

Clinical presentation: Common signs include loud snoring, excessive daytime sleepiness, and fatigue. Patients with OSA are often obese, and many have resistant hypertension. They may also present with different arrhythmias, including paroxysmal supraventricular tachycardia, non-sustained ventricular tachycardia, sick sinus syndrome, heart block, and heart failure with preserved ejection fraction (HFpEF).

Diagnosis: Diagnosis is confirmed through polysomnography or home sleep apnea testing. A simplified polysomnogram confirms the diagnosis (apnea–hypopnea index (AHI) > 5) and can quantify the severity of obstructive sleep apnea syndrome (OSAS) (mild: AHI <15; moderate: AHI of 15–30; severe: AHI >30)

Treatment: The primary treatment is positive airway pressure (PAP) therapy. Weight loss, application of nasal continuous positive airway pressure (CPAP) machines, and sometimes surgical interventions (e.g., uvulopalatopharyngoplasty) are recommended.[137]

Coarctation of the Aorta[129]

Pathophysiology: Coarctation of the aorta is a congenital narrowing of the aorta, leading to higher BP in the upper extremities and lower BP in the lower extremities. The increased pressure in the upper body stimulates the RAAS, contributing to hypertension.

Clinical presentation: Symptoms may include leg weakness, cold extremities, and hypertension that is often more severe in the arms than in the legs. Aortic bruit may be heard.

Diagnosis: Echocardiography, MRI, or CT angiography can identify the narrowing of the aorta.

Treatment: Surgical correction or balloon angioplasty is typically required for long-term management.

Other Causes

Acute stressful situations cause intense sympathetic discharge and may temporarily induce hypertension. In such situations, treatment with beta blockers is preferred. Common conditions include acute mental stress, hypoglycemia, acute intermittent porphyria, exposure to cold, burns, perioperative period, and post-head injury.

Drugs: NSAIDs, sympathomimetic amines, ephedrine, glucocorticoids, cocaine, and amphetamines can all cause significant hypertension. Anticancer drug therapy can also cause hypertension. Tyrosine kinase inhibitors and proteasome inhibitors also increase BP, as do adjuvant therapies (corticosteroids, calcineurin inhibitors, and antiandrogen hormone therapy). Hypertension caused by anticancer drugs is often dose-limited and may be reversible after therapy discontinuation. Hypertension in these patients is managed with the same principles as for primary hypertension.

Complications

The complications of hypertension can be considered either hypertensive or atherosclerotic. Although the extent of damage often correlates with the level of BP, this is not always the case. BP and organ impairment should be evaluated separately. The various complications are as follows:

Hypertensive Heart Disease

Hypertension has the following effects on the heart: left ventricular hypertrophy (LVH), increased risk of coronary artery disease, arrhythmias, congestive cardiac failure (HFpEF and HFrEF), and sudden cardiac death.[138]

Most episodes of left ventricular failure in hypertensive patients are associated with diastolic heart dysfunction (HFpEF).

Treatment of hypertension can reverse ventricular hypertrophy.[139,140] However, the impact of the reduction of LVH on the reduction of morbidity and mortality is still debated.

Cerebrovascular Disease

Hypertension is the most important modifiable risk factor for all types of atherothrombotic strokes.[141] and intracerebral hemorrhage caused by the rupture of Charcot–Bouchard aneurysms.

The relationship between the incidence of stroke and BP is continuous.[142,143] A 5–6 mm Hg reduction in diastolic blood pressure reduces the risk of stroke by 40%.[144] The systolic hypertension elderly program (SHEP) study showed substantial benefit following control of systolic BP in the elderly.[30]

Kidney Disease

- About 20–25% of renal failure cases are attributed to uncontrolled hypertension.[145]
- Development of renal damage is preceded by microalbuminuria, which progresses to overt proteinuria and may further progress to end-stage renal disease.[146]
- The reduction of proteinuria can be achieved through effective BP control, especially with use of ACE inhibitors and ARBs.[147,148]

Retinopathy

Hypertensive retinopathy is a condition characterized by a spectrum of retinal vascular signs in people with elevated BP.

The classification of Keith, Wagener, and Barker has been widely used. Grade I retinopathy is characterized by copper wire appearance; Grade II by arteriovenous nipping; Grade III by the presence of hemorrhages and exudates; and Grade IV by papilledema.

Grade III and IV retinopathy is seen in cases of long-standing uncontrolled hypertension. These changes may regress with the effective control of BP.

Several reviews of hypertensive retinopathy since 1996 have questioned the usefulness of the classification system by Keith et al. and its relevance to current clinical practice. Recent studies show that some of the retinal signs (e.g., hemorrhages, microaneurysms, and cotton-wool spots) predict stroke and death from stroke independently of elevated blood pressure and other risk factors.[149]

Large Vessel Disease

Hypertension is a risk factor for the development of intermittent claudication due to peripheral vascular disease. It also increases the risk of abdominal aortic aneurysms and aortic dissection. Eighty percent of patients with aortic dissection have hypertension.[150]

Acute Severe Hypertension: Emergency and Nonemergency

Our guidelines have changed the terminology of accelerated and malignant hypertension to acute severe hypertension: emergency and nonemergency, respectively, so as to reduce the confusion around these terms.

Acute-severe hypertensive emergency (malignant hypertension) is characterized by severe elevations in BP (>180/120 mm Hg) complicated by evidence of impending or progressive target organ dysfunction. Such cases require immediate BP reduction (not necessarily to normal), often with parenteral agents over a period of 6–8 hours with constant monitoring, to prevent or limit HMOD.

Examples include hypertensive encephalopathy, intracerebral hemorrhage, acute MI, acute left ventricular failure with pulmonary edema, unstable angina pectoris, aortic dissection, acute kidney injury, or eclampsia.[151,152] Intravenous nitroglycerine is generally used, although it is not very effective, but it is especially useful in patients with ischemic heart disease and left ventricular failure.[153] The recommended dose is 5 µg/min initially, followed by titration at 5 µg/min at 3-to-5-minute intervals, up to 10 µg/min. Intravenous enalaprilat is useful in hypertensive emergencies, especially in the presence of heart failure. It is administered as a 0.625–1.25 mg bolus dose every 6 hours. Meanwhile, intravenous labetalol is also being used in hypertensive emergencies as a bolus dosage of 2–10 mg and infusion of 2.5–30 µg/kg/min. Intravenous esmolol has been shown to be especially useful for perioperative accelerated hypertension. The usual bolus dose is 80–500 µg/kg over 1 minute, followed by an infusion of 50–300 µg/kg/min. Finally, intravenous nitroprusside is rarely required and is only administered in cases of dissection of the aorta or subarachnoid hemorrhage with very high BP. Its administration requires an intensive care setting and very close monitoring. The dose is 0.3 µg/kg/min to a maximum of 4 µg/kg/min. Sublingual captopril can also be used when a less rapid reduction is required.

Acute-severe hypertensive non-emergency (accelerated hypertension) is a situation associated with severe elevations in BP without progressive target organ dysfunction.

Examples include upper levels of stage II hypertension associated with severe headache, shortness of breath, epistaxis, or severe anxiety. The majority of these patients present as noncompliant or inadequately treated hypertensive patients, often with little or no evidence of HMOD. The aim should be the safe, prompt, and gradual lowering of BP with oral medication over a period of 1–3 days.[153] In most situations, BP can be controlled with rapidly acting oral medications such as CCBs and ACE inhibitors/ARBs.

Sublingual nifedipine should not be used in hypertensive crises as it can cause a precipitous fall in BP, reflex tachycardia, and may precipitate renal, cerebral, or coronary ischemia.[154]

Hypertension in Special Subsets

Hypertension with Diabetes

Around 30 to 35% of individuals with hypertension have coexisting diabetes mellitus (both type 1 and type 2). Similarly, the prevalence of hypertension is 1.5 to 2 times higher in individuals with diabetes mellitus than in nondiabetic persons.[6] Interestingly, increased BP may inherently increase the risk of diabetes, underscoring the significance of BP reduction in avoiding diabetes in addition to reducing CV risk. Diabetes is also a major cause of microvascular events, such as retinopathy and nephropathy.[5] The coexistence of diabetes and hypertension leads to increased cardiovascular morbidity and death.

Diagnosis

In diabetes patients, BP should be assessed at every visit, adhering to the same measurement methodology as that used for typical hypertensive patients. In the diabetic population, it is essential to assess BP in supine, sitting, and standing positions to rule out the possibility of autonomic neuropathy.[6]

Threshold and Target of Treatment

In patients with high-normal BP with diabetes mellitus, more aggressive lifestyle measures should be followed with a low threshold to start pharmacotherapy. In case of BP of more than 140/90 mm Hg (any stage of hypertension) pharmacotherapy should be started to achieve cardiovascular and microvascular protection.

Patients with diabetes should be given BP-lowering drugs with a BP goal of 120–129/70–79 mm Hg, if possible.[5]

Management

Lifestyle modifications must be vigorous in diabetic hypertensive patients. Weight reduction in obese and dietary alterations like reduced salt and fat intake are recommended. Consistent exercise forms the foundation of lifestyle modifications and is suitable at all stages of hypertension.[6]

Treatment

A combination of two or more drugs is usually required for controlling the BP to achieve target levels.

ACE inhibitors (HOPE trial)[155] and ARBs (ONTARGET trial)[156] have demonstrated the importance of RAAS blockade in reducing the risk of diabetes complications, especially microvascular complications and macrovascular complications. ACE inhibitors and ARBs are beneficial in preventing new-onset diabetes and can be considered in individuals at risk of diabetes who are eligible for BP-lowering treatment.[6] Albuminuria is more prevalent in diabetes, and therefore, ACE inhibitors and ARBs offer potential benefits that may justify BP-lowering in patients with diabetes.[5] ACE inhibitors and ARBs are first-line therapy in type 1 or type 2 diabetes patients.[6]

CCBs have been found to be helpful as monotherapy and in combination with ACE inhibitors. The combination of amlodipine and perindopril is associated with a significantly lower risk of new-onset diabetes as compared to the combination of a β-blocker and diuretic.[6]

β-blockers potentially mask hypoglycemic symptoms. The use of β-blockers in diabetic patients with symptoms of CAD and congestive heart failure may be extremely helpful. Cardioselective β-blockers like nebivolol and carvedilol should be preferred.[6]

The drugs that are beneficial in pregnant woman with diabetes who are also hypertensive include methyldopa, calcium channel blockers, and labetalol. The use of ACE inhibitors/ARBs is contraindicated. The use of diuretics during pregnancy can lead to a reduction of plasma volume which can result in low perfusion, leading to decreased fetal growth/fetal damage.[6]

SGLT-2 inhibitors (empagliflozin, canagliflozin and dapagliflozin) have been evaluated recently amongst diabetic patients in three large trials (EMPA-REG, CANVAS Program and DECLARE-TIMI 58). These agents have significant CV benefits and reduce BP. They reduce BP significantly in patients with diabetes or hypertension, irrespective of the level of BP. This is a class effect seen with all these three agents. The EMPA-REG trial noted a 38% relative risk reduction for death from CV causes and 35% risk reduction in hospitalization for heart failure. A significantly reduced progression of kidney disease and renal events was also observed with these agents.[6]

Hypertension with Cerebrovascular Disease

Hypertension is a critical risk factor for cerebrovascular diseases, including stroke and vascular cognitive impairment. It is associated with over 50% of ischemic and 70% of hemorrhagic strokes. Despite effective BP management, the 10% residual risk of recurrent cerebrovascular events highlights the complex interplay between BP regulation and cerebrovascular health.[157] Hypertension may also result in the hemorrhagic conversion of an ischemic stroke.[158]

Hypertension and Stroke Risk

Hypertension is a primary modifiable risk factor for stroke, influencing both ischemic and hemorrhagic subtypes. Elevated and variable BP levels directly contribute to cerebral vessel damage, leading to increased susceptibility to strokes. This underscores the necessity for consistent and comprehensive BP control across all populations to reduce the long-term risks of cerebrovascular complications.[159,6] The recommended BP for stroke patients should be below 140/90 mm Hg. A 10 mm Hg decrease in blood pressure correlates with a one-third reduction in stroke risk for primary prevention.[159]

Pathophysiological Mechanisms

The relationship between hypertension and cerebrovascular disease is driven by several pathophysiological mechanisms:

Arterial stiffness and increased pulsatility: Hypertension causes arterial stiffness and heightened pulsatility, which leads to greater strain on cerebral vessels, increasing the risk of cerebrovascular injuries. These changes are central to the pathogenesis of both ischemic and hemorrhagic strokes.[157]

Blood pressure variability: Variability in BP readings, even when average levels are controlled, significantly predicts the risk of ischemic and intracerebral hemorrhages. Fluctuations in BP amplify endothelial damage, further predisposing individuals to cerebrovascular events.[157]

Cerebral small vessel disease: Chronic hypertension accelerates SVD, a condition associated with impaired vascular reactivity and increased pulsatility. This contributes to cognitive decline and recurrent strokes, highlighting the importance of targeted therapeutic interventions.[157]

Impaired cerebral blood flow regulation: Hypertension disrupts the brain's autoregulatory mechanisms, reducing its ability to adapt to changes in systemic BP. Impaired responses to carbon dioxide have been observed in hypertensive individuals, further increasing the risk of cerebrovascular injury.[157]

Hypertensive encephalopathy is an emergency that needs to be identified, and BP has to be aggressively managed in these cases.[6]

In acute cerebrovascular disease, the goal is to gradually reduce the blood pressure and carefully monitor it for the first 24 hours in view of the possibility of transient hypotension.[6]

Treatment of acute BP elevation in cerebral hemorrhage has been addressed in two trials. The INTERACT 2 (2013),[160] the ATACH II (2016),[161] and INTERACT3 (2021)[162] trials have both explored the benefits of intensive BP lowering in patients with acute cerebral hemorrhage. The first two trials show that early intensive lowering to less than 140 mm Hg, as compared to a target of <180 mm Hg, has no mortality benefit, although there was some improved functional outcome whereas the INTERACT3 trial showed that intensive blood pressure lowering within several hours of symptom onset improved functional outcomes in patients with intracerebral hemorrhage. We recommend immediate initiation of antihypertensive therapy within 6 hours of symptom onset to maintain a target systolic BP of 140–160 mm Hg, to prevent hematoma expansion and improve functional outcomes.

- Immediately after the occurrence of an ischemic cerebral infarction, it is appropriate to withhold treatment in patients who present with high BP, unless blood pressure is very high (>220/120 mm Hg). In such patients a cautious reduction in BP by 10 to 15% only is suggested during the next 24 hours.[6]
- BP should not be aggressively reduced in ischemic stroke patients who are otherwise not candidates for thrombolysis. In patients who are candidates for thrombolytic therapy, systolic BP of >185 mm Hg and diastolic BP of >110 mm Hg should be actively treated, and BP should be maintained below 185/105 mm Hg over the next 24 hours.[6]
- In poststroke patients, the evidence for long-term reduction in incidence of stroke after control of BP has been consistent. In clinical trials, antihypertensive therapy has been associated with an average reduction of 35% to 40% in stroke incidence. In stroke survivors with hypertension, BP-lowering therapy has been shown to yield a 43% reduction in stroke recurrence.[6]
- Earlier guidelines recommended using ACE inhibitors/ARB plus a calcium channel antagonist or thiazide/thiazide-like diuretic, starting immediately after a transient ischemic attack (TIA) and within a few days of ischemic stroke.[5]
- In the PROGRESS TRIAL, the combination of perindopril and indapamide reduced the risk of stroke by 43% among patients who were hypertensive or normotensive. Perindopril alone was not found to have a similar reduction in the risk of stroke. Hence, the combination of an ACE inhibitor and a diuretic is preferable.[6]

Hypertension with Chronic Kidney Disease

Hypertension is both the leading cause and a consequence of CKD. The effective management of hypertension in CKD is critical not only to prevent progression to end-stage renal disease (ESRD) but also to mitigate CV risks, which are a major cause of morbidity and mortality in these patients. Diabetic nephropathy, hypertensive nephropathy, and chronic pyelonephritis cause about 30%, 10%, and 10% of CKD cases, respectively (Table 29).[163]

There are two forms of kidney diseases causing hypertension, namely renal parenchymal and renovascular disease.

Causes

- Renal parenchymal diseases.
  - Chronic glomerulonephritis.
  - Chronic interstitial nephritis.
  - Analgesic nephropathy.
  - Polycystic kidney disease.
  - Gout with renal failure.
  - Obstructive nephropathy.
  - Renovascular hypertension (discussed in Secondary Hypertension)

Treatment

In CKD, therapy with antihypertensive drugs has been found to not only control BP but also slow down the renal damage. The Ramipril Efficacy in Nephropathy (REIN), ACE Inhibitors and progressive Renal Insufficiency (AIPRI) and modification of Dietary Protein in Renal Disease (MDRD) trials established the ability of antihypertensives to slow down the progression of non-diabetic CKD.[163]

Threshold for the initiation of antihypertensive treatment:

- BP >140/90 mm Hg for patients without proteinuria.
- BP >130/80 mm Hg for those with proteinuria.
- Target BP is <130/80 mm Hg.

In postrenal transplant patients, hypertension is an important issue since certain drugs used in these patients, like cyclosporine and erythropoietin, can aggravate hypertension. At times, the combination of multiple drugs, including ACE Inhibitors/ ARBs, CCBs, and diuretics, may be required for effective BP control. In patients where BP is still not controlled, clonidine, α-methyl dopa, or α-blockers may be added.[163]

Updated Treatment Recommendations

The management of hypertension in CKD patients has evolved significantly, guided by advances in research and new clinical insights. The 2023 European guidelines have been pivotal in refining therapeutic approaches to better cater to the unique needs of CKD patients.

Novel Therapeutic Agents

The introduction of new drug categories has broadened the arsenal available for treating hypertension in CKD. These include:

- Neprilysin receptor antagonists: These agents target the natriuretic peptide system, reducing BP while offering renoprotective effects.[163]
- Sodium–glucose transporter-2 (SGLT-2) inhibitors: Initially developed for diabetes

Table 29: Stages of chronic kidney diseases and action plan[163]

Stage	*Description*	*GFR (mL/min per 1.73 m^2)*	*Action*
–	At increased risk for CKD	≥90 with risk factors	Screening for CKD risk reduction
1	Kidney damage with normal or increased GFR	≥90	Diagnosis and treatment. Retard progression of CKD, treat comorbidities. Cardiovascular disease risk reduction
2	Mild decrease in GFR	60–89	Estimate progression
3a	Mild to moderate decrease in GFR	45–59	Evaluate and treat complications
3b	Moderate to severe decrease in GFR	30–44	
4	Severe decrease in GFR	15–29	Prepare for renal replacement therapy
5	Kidney failure	< 15 or dialysis	Renal replacement therapy if uremic

GFR: glomerular filtration rate

management, SGLT-2 inhibitors have demonstrated profound benefits in reducing CKD progression, particularly in patients with albuminuria.[163]
- Nonsteroidal mineralocorticoid receptor antagonists (MRAs): Unlike traditional MRAs, these newer agents, such as Finerenone, minimize the risk of hyperkalemia while effectively controlling BP and albuminuria.[163]
- Glucagon-like peptide-1 receptor Agonist (GLP-1RA) like Semaglutide, as per the SOUL study, reduced the major adverse cardiac event rate by 14% in patients with cardiorenal metabolic disease.[164]

Stepwise Drug Selection Algorithm

The updated guidelines emphasize a step-by-step approach for selecting antihypertensive medications based on CKD stage and comorbidities:

- *Initial therapy:* ACE inhibitors or ARBs remain the cornerstone of treatment, particularly for patients with albuminuria.[165]
- *Combination therapy:* For patients not achieving target BP, combining ACE inhibitors or ARBs with diuretics or CCBs is recommended.[165]
- *Resistant hypertension:* In cases of resistant hypertension, the guidelines advocate adding spironolactone or other MRAs, along with evaluating secondary causes.[165]
- *Blood pressure targets:* Targets are individualized, with stricter goals for patients with high albuminuria levels.[165]

Hypertension with Hyperuricemia

The prevalence of hyperuricemia in hypertensive patients ranges from 20 to 40%,[166] and a similar prevalence of hypertension is found in patients with gout (25%–50%).[167] Higher uric acid levels are associated with hypertension-related target organ damage, such as renal function impairment, left ventricular hypertrophy, and subclinical myocardial damage.[168]

The LIFE study[169] showed that treatment of hypertension with losartan lowered the urate levels compared to atenolol. Therefore, for patients with hypertension and hyperuricemia losartan may be the preferred antihypertensive agent because it reduces serum uric acid and gout risk. Calcium channel blockers (CCBs), especially amlodipine, may be an alternative. Thiazide diuretics should generally be avoided as they increase uric acid levels and gout risk. Treatment for hyperuricemia needs to be started along with antihypertensives where indicated.

Hypertension with Ischemic Heart Disease

High systolic BP is a key risk factor for IHD that significantly elevates morbidity and mortality globally.[170] Individuals with hypertension face a 6–8 fold increase in the odds of IHD mortality.[170] Elevated systolic BP exerts continuous mechanical stress on arterial walls, leading to endothelial dysfunction, arterial stiffness, and accelerated atherosclerosis, all of which contribute to CAD and MI.

The Threshold of Risk

The risk of IHD begins to rise even at systolic BP levels traditionally considered normal, such as 120/80 mm Hg.[170] Untreated individuals are at an especially high risk, as their elevated BP levels persist unchecked, causing cumulative CV damage over time. These findings underscore the need for early and consistent BP management as a preventive measure against IHD.

Impact of Hypertension Treatment on Ischemic Heart Disease

While antihypertensive therapy significantly reduces CV risk, it does not completely eliminate the residual risk of CHD. The Isfahan Cohort Study revealed that individuals with treated hypertension still exhibit a higher risk of CVD compared to those with optimal BP levels.[171] This phenomenon emphasizes the importance of comprehensive strategies that extend beyond BP control to address the broader spectrum of CV risk.

Additional Risk Factors Amplifying Hypertension-related IHD

Hypertension rarely acts in isolation while contributing to IHD. It interacts with other major cardiovascular risk factors, such as dyslipidemia, obesity, and diabetes, to compound the overall burden of disease.

Lifestyle Interventions

Lifestyle modifications form the cornerstone of effective hypertension and IHD management. Dietary changes, such as adopting a low-sodium, high-potassium diet rich in fruits, vegetables, and whole grains, have been shown to significantly lower BP and improve CV health. Regular physical activity and weight management further enhance these benefits, reducing the overall CV risk profile of hypertensive individuals.

Management

- Excessively rapid lowering of BP can cause reflex tachycardia and sympathetic activation and should be avoided in patients with CAD.
- One may have to set the target of BP control even below 130/80 mm Hg, but not lower than 120/70 mm Hg. The CLARIFY registry (2016) showed that BP levels below 120 mm Hg systolic and 70 mm Hg diastolic were associated with adverse CV outcomes, including mortality, supporting the existence of a J-curve phenomenon.[172,173] All other risk factors should be treated appropriately.
- Hypertension in patients with acute coronary syndrome should be treated aggressively.
- β-blockers and CCBs are the drugs of first choice in the management of angina in patients with hypertension associated with CAD.
- β-blockers have been shown to reduce the risks of reinfarction and CV death by 25% in patients with MI.[174]
- Amlodipine has been shown to produce subjective and objective improvement in patients with angina.[175] Treatment with amlodipine is associated with fewer hospitalizations for unstable angina and revascularizations in patients with angiographically documented CAD.[176]
- Verapamil and diltiazem reduce the risk of developing MI following non-Q-wave myocardial infarction.[177]
- After MI, therapy with ACE inhibitors and ARBs prevents subsequent heart failure and reduces morbidity and mortality.[178] ACE inhibitors in combination with low-dose diuretics are effective in reducing morbidity and mortality in patients in heart failure.[179]
- Statins and aspirin are recommended in patients with hypertension associated with CAD.

Hypertension with Congestive Cardiac Failure

Hypertension is a primary modifiable risk factor for the development of heart failure, whereas the advancement of heart failure typically exacerbates hypertension, producing a vicious cycle. Elevated BP induces structural and functional cardiac remodeling, including left ventricular hypertrophy, diastolic dysfunction, and eventually, systolic failure, leading to congestive symptoms.[180] The left ventricular diastolic dysfunction may be a sign of diverse combinations of cardiovascular, metabolic, pulmonary, renal, and geriatric diseases. Patients with heart failure have historically been categorized into three groups based on their left ventricular ejection fraction (LVEF): heart failure with reduced ejection fraction <40% (HFrEF), heart failure with mildly reduced ejection

fraction (HFmrEF) with LVEF between 41 and 49%, and heart failure with preserved ejection fraction (HFpEF) with an LVEF ≥ 50%. Women are more prone to acquire HFpEF, rather than HFrEF, as compared to males.[181]

Management Strategies

Nonpharmacological Approaches

Lifestyle modifications, including weight reduction, sodium restriction, physical activity, smoking cessation, and a heart-healthy diet (e.g., DASH diet), are foundational.

Pharmacological Approaches

Inhibition of the renin-angiotensin system is advised to minimize morbidity and mortality for patients with HFrEF, and ARNI, ACE inhibitors, or ARBs are recommended as first-line treatment.[182] Recent data from the PARADIGM- HF study show that the ARNI sacubitril/valsartan is superior to enalapril in reducing the risks of death and of hospitalization for heart failure.[6]

In patients with CCF stabilized with ACE inhibitors and diuretics, selective β-blockers such as metoprolol or bisoprolol, and the α-β blocker carvedilol may be given as appropriate. The use of these β-blockers has been demonstrated to lower mortality. These medications should be initiated in modest dosages and then progressively increased, as tolerated.[6]

In patients with severe hypertension and acute left ventricular failure, BP needs to be brought down fast to normal or slightly above the normal range. This can be done by injection of intravenous drugs such as furosemide, nitroglycerine, enalaprilat, or sodium nitroprusside.[6]

Amlodipine has been shown to be safe in treating hypertensive individuals with angina and left ventricular failure, when coupled with ACE inhibitors, low-dose diuretics, and digoxin. Other CCBs are not advised in these patients.[6]

Sacubitril–valsartan may be effective in treating apparent resistant hypertension in patients with HFpEF, even in those who continue to have a high BP despite therapy with at least four antihypertensive medication classes, including MRAs.[183]

Hypertension with Atrial Fibrillation

Hypertension is a significant risk factor for atrial fibrillation (AF), a common arrhythmia associated with increased risks of stroke, heart failure, and mortality.[184]

Epidemiology

AF affects approximately 1% of the global population, with its prevalence increasing with age and in individuals with hypertension. Nguyen Tung's study indicates that up to 25% of hypertensive patients develop AF over their lifetime.[185] In India, the growing prevalence of hypertension coupled with the underdiagnosis of AF poses a significant public health challenge, necessitating improved screening and management approaches.

Pathophysiology of Hypertension and Atrial Fibrillation

Hypertension predisposes individuals to AF through several interrelated mechanisms:

- *Structural remodeling*: Chronic hypertension leads to LVH and left atrial enlargement. These structural changes promote atrial fibrosis and disrupt electrical conduction, creating a substrate for AF.[186]
- *Electrical remodeling*: Altered ion channel expression and shorter atrial action potentials in hypertensive patients increase susceptibility to arrhythmias.
- *Neurohormonal activation*: RAAS activation in hypertension promotes atrial fibrosis and inflammation, contributing to AF.[187]
- *Endothelial dysfunction*: Hypertension-induced endothelial damage and oxidative stress increase thromboembolic risks in AF patients.
- *Autonomic nervous system dysregulation*: Heightened sympathetic activity in hypertensive individuals exacerbates atrial electrical instability and arrhythmogenesis.

Clinical Implications

The cooccurrence of hypertension and AF leads to severe clinical consequences, including:

- *Increased stroke risk:* AF and hypertension synergistically heighten thromboembolic risk, significantly increasing the likelihood of ischemic stroke.[186]
- *Heart failure:* Hypertension contributes to left ventricular dysfunction, which, when coupled with AF, accelerates the progression to heart failure.
- *Higher mortality rates:* Pittaras et al. demonstrated that hypertensive patients with AF face increased risks of mortality, especially those with low cardiorespiratory fitness.[187]

Screening and Diagnosis

The early detection of AF in hypertensive patients is critical for reducing complications. Effective screening strategies include:

- *Routine ECG screening*: Hypertensive patients, particularly those over 65 years of age, should undergo regular ECGs to identify AF.
- *Ambulatory blood pressure monitoring (ABPM)*: ABPM aids in detecting masked or white-coat hypertension, which is a risk factor for AF.
- *Holter monitoring*: For patients with paroxysmal AF, 24-hour Holter monitoring can confirm arrhythmic episodes.
- *Wearable devices*: Modern wearable devices with ECG capabilities provide a practical means of detecting asymptomatic or intermittent AF.

Oscillometric BP monitors are not always reliable in the presence of AF, due to the increased beat-to-beat fluctuation of BP beat-to-beat, hence additional auscultatory measures are needed. Some oscillometric BP monitors incorporate an algorithm for identifying AF, although an ECG is still necessary to confirm the diagnosis.[5]

Evidence-based Management

The management of hypertensive patients with AF requires a multidisciplinary approach to address both conditions effectively.

Blood pressure control: Maintaining optimal BP levels is vital to reducing AF risk and recurrence. Studies suggest targeting a systolic BP of <130 mm Hg.[186]

Preferred Antihypertensives

- *RAAS inhibitors*: ACE inhibitors and ARBs provide antiremodeling effects.
- *Beta-blockers*: Effective for rate control in cases of coexisting AF.
- *Calcium channel blockers*: Useful in managing both BP and for rate control of AF (diltiazem/verapamil).

Anticoagulation Therapy

- Anticoagulation is essential for preventing thromboembolism in hypertensive AF patients with CHA_2DS_2-VASc scores.[186]
- Direct oral anticoagulants (DOACs) like apixaban, rivaroxaban, dabigatran or edoxaban are preferred over warfarin due to their superior safety and efficacy profiles.[185]
- Vitamin K antagonist–warfarin or dicoumarol can be used in dosages so as to keep the INR between 2–3.[6]

Rhythm and Rate Control

- *Rate control*: Medications such as beta-blockers, diltiazem, or verapamil help maintain an appropriate ventricular rate.
- *Rhythm control*: Antiarrhythmics, such as amiodarone, flecainide, and catheter ablation may be employed in symptomatic AF patients.

Lifestyle Modifications

- Lifestyle changes, including weight reduction, regular exercise, dietary sodium restriction, and alcohol moderation, have shown significant benefits in reducing AF burden.[187]

Hypertension with Chronic Obstructive Pulmonary Disease

Hypertension and chronic obstructive pulmonary disease (COPD) frequently coexist in individuals, attributable to common risk factors such as tobacco use, advancing age, and systemic inflammatory responses. Approximately 25–50% of individuals with COPD are also diagnosed with hypertension.[188] Hypertension is often precipitated by the use of systemic steroids, β-agonists, or nasal decongestants. Stress also plays a significant role in the development of hypertension in these patients.[6]

Management

The concurrent management of COPD and hypertension is imperative, as untreated hypertension may heighten CV risks, while inadequately managed COPD can exacerbate systemic inflammation, thereby facilitating the progression of hypertension.[189] Both conditions considerably diminish the quality of life and escalate healthcare expenditures if not effectively managed.[190]

Medication Considerations for Managing Hypertension in COPD

Long-acting CCBs such as amlodipine have been found safe in this group of patients.

ACE inhibitors and the cough conundrum: ACE inhibitors are efficacious antihypertensives; however, they may induce a persistent dry cough, which could be misinterpreted as deterioration in COPD symptoms.[191] It is recommended that if a cough develops, ARBs should be tried as an alternative to ACE inhibitors.[6]

Beta-blockers: Historically, the use of beta-blockers in COPD patients was discouraged due to concerns regarding bronchoconstriction. Newer selective beta-blockers, i.e., cardio-selective beta-blockers such as metoprolol and bisoprolol, have demonstrated both safety and efficacy in individuals with COPD.[192] These pharmacological agents effectively mitigate hypertension and CV risks without significant adverse respiratory effects. Regular surveillance of respiratory and CV parameters is advocated when prescribing beta-blockers.[193]

Diuretics and electrolyte monitoring: Diuretics are frequently employed in the treatment of hypertension; however, they may precipitate electrolyte disturbances, notably hypokalemia, which poses significant risks in COPD patients.[194]

Tachycardia and hypertension in COPD: Frequently prescribed pharmacotherapeutics for COPD, such as beta-agonists and phosphodiesterase inhibitors, possess the potential to precipitate tachycardia, thereby complicating the management of concomitant hypertension.[195]

- *Choosing heart rate-controlled antihypertensives:* CCBs such as diltiazem demonstrate efficacy in the management of hypertension while simultaneously regulating heart rate, thereby providing dual therapeutic benefits for this specific patient population.[196] However, before its use, the assessment of RV function is warranted as these drugs can worsen RV dysfunction.
- Inhaled corticosteroids and ipratropium bromide can be used safely in these patients.[6]

Hypertension with Dyslipidemia

Dyslipidemia often coexists with hypertension.[6] Up to 40% of newly diagnosed hypertensive patients have at least one lipid abnormality.[197]

Management strategies

Nonpharmacological

Lifestyle modification is the foundation of interventions for lowering BP and improving lipid levels.[6]

Pharmacological

Antihypertensive medicines should be prescribed considering the lipid profile.

ACE inhibitors and CCBs are preferred as they are lipid-neutral. High-dose diuretics can generate a short-term rise in cholesterol, triglycerides, and LDL cholesterol levels. However, low-dose thiazides do not produce this effect.[6] The RAAS blockers or CCBs should be the preferred as initial therapy in patients with underlying hyperlipidemia.[197]

Notably, beta-blockers without intrinsic sympathomimetic action (ISA) may raise the levels of plasma triglycerides and diminish the levels of HDL-cholesterol.[6] Nevertheless, these have been shown to reduce the rate of sudden death, overall mortality, and recurrent MI in patients with previous MI.

Similar to patients with CVD and diabetes, patients with hypertension and dyslipidemia also require lipid-lowering therapy (statins).[6]

Hypertension in Women and Pregnancy

Hypertension in Women

Some of the side effects of commonly used drugs, such as ACE inhibitor-induced cough, CCB-induced pedal edema, and diuretic-induced hyponatremia and hypokalemia, are seen more often in women than in men.[6]

Estrogen–progesterone oral contraceptive pills induce a marked rise in systolic (and to a lesser extent, diastolic) BP. 5% of women who have used the pill for 5 years develop hypertension. Age, positive family history, a history of pregnancy-induced hypertension, and obesity are established risk factors for pill-induced hypertension. In more than half of all patients, BP returns to normal after the pill is discontinued.[6]

Hormone replacement therapy (low-dose estrogen) in postmenopausal women is no longer indicated.

Hypertension in Pregnancy

Hypertension in pregnancy is the second leading cause of maternal mortality after maternal peripartum hemorrhage. About 7% of pregnancies are complicated by hypertension, of which 3% are related to pre-eclampsia, and roughly 1% are due to chronic or pre-existing hypertension. Women with a history of hypertensive disorders during pregnancy are at a greater risk of later hypertension and CVD.[5] Maternal hazards include placental abruption, stroke, multiorgan failure, and disseminated intravascular coagulation. The fetal hazards include intrauterine growth retardation as well as preterm and intrauterine mortality.[6] About 20–30% of women with hypertension problems in a previous pregnancy will develop recurrence in a later pregnancy.

Hypertension in pregnancy is commonly defined as systolic BP of ≥140 mm Hg and/or diastolic BP of ≥90 mm Hg, evaluated via repeated BP readings on two different occasions or ≥15 min apart in cases of severe hypertension (≥160/110 mm Hg).[5]

Hypertension in pregnancy includes:

- *Chronic hypertension*: Predates pregnancy, occurs before 20 weeks of gestation, persists for >6 weeks post-partum, and may be accompanied by proteinuria.[5,6]
- *Gestational hypertension:* Occurs after 20 weeks of gestation and normally disappears within 6 weeks postpartum. This is not associated with significant proteinuria.[5,6]
- *Preeclampsia:* Gestational hypertension accompanied with the onset of (a) proteinuria (>0.3 gm/day or ≥30 mg/mmol ACR); (b) maternal organ dysfunction, including acute kidney damage, liver dysfunction, neurological problems (convulsions, altered mental status, blindness, stroke, severe headaches, and persistent visual scotomata), or hematological issues (platelet count < 150,000/μL, disseminated intravascular coagulation, hemolysis);

or (c) uteroplacental dysfunction (such as fetal growth restriction, abnormal umbilical artery Doppler waveform analysis, or stillbirth). The only remedy for preeclampsia is delivery, which is suggested at 37 weeks' gestation, or earlier in high-risk patients.[5,6]

- *Antenatally unclassifiable hypertension:* BP is initially measured after 20 weeks of gestation, and hypertension is identified, but it is unclear if it is chronic or not; evaluation is essential at 6 weeks postpartum.[5,6]

Diagnosis

Pre-eclampsia superimposed over pre-existing hypertension in pregnancy is detected by recording phase IV or V of Korotkoff sounds with the patient lying in a lateral posture. Manual auscultation is the method of choice, as automated BP devices are unreliable in pregnancy and preeclampsia.[6]

Basic laboratory investigations include urinalysis, blood count, hematocrit, liver enzymes, serum creatinine, and serum uric acid. Serum uric acid is increased in pre-eclampsia and identifies women at increased risk. All pregnant women should be assessed for proteinuria in early pregnancy. The Urine ACR, which can be quickly determined in a single spot-urine sample, should be examined.

Treatment

Lifestyle changes like guarded exercises are recommended, but a salt-limited diet is not recommended.[6]

Low-to-moderate-intensity exercise should be initiated during the first trimester of pregnancy to reduce the risk of developing hypertension. All pregnant women should participate in physical activity, unless contraindicated.

Women with a moderate to high risk of preeclampsia (prior eclampsia, CKD, diabetes mellitus, chronic hypertension, autoimmune illnesses, multiple pregnancy, maternal age >40 years) should start on aspirin 100–150 mg from the 12th to 36th weeks of pregnancy.[6]

For mild hypertension in pregnancy, the initiation of antihypertensive medicines is evaluated if the BP is ≥140/90 mm Hg combined with gestational hypertension or subclinical HMOD or in any patient with BP ≥150/95 mm Hg. A BP goal of < 140/90 mm Hg has been recommended. Antihypertensive drugs significantly decrease the incidence of severe hypertension by 40–60%.[6]

Methyldopa is suggested for women whose hypertension is first diagnosed during pregnancy. Calcium channel blockers (nifedipine), labetalol, or hydralazine can also be utilized.[6]

ACE inhibitors and ARBs are contraindicated in pregnancy. Sodium nitroprusside is contraindicated due to the possibility of fetal cyanide poisoning. Use of low-dosage diuretics is discouraged, as preeclampsia is a volume-depleted condition.[6]

A 2014 meta-analysis evaluated maternal and fetal outcomes from 49 randomized trials of treatment versus no treatment in women with mild hypertension (140–159/90–109 mm Hg) during pregnancy. The results showed that treatment did not result in either fetal benefit or harm. In 2015, the CHIPS trial (control of hypertension in pregnancy) randomly assigned pregnant women with gestational or chronic hypertension to diastolic BP treatment targets of 85 mm Hg (tight control) or 100 mm Hg (less tight control), and demonstrated no differences in maternal, fetal, or neonatal outcomes among the two groups. Although fewer women in the tight control group developed severe hypertension. However, there was no overall effect on perinatal morbidity or mortality.[6] Based on the findings of the CHIP trial, 140/90 is used as the threshold for initiation or titration of medical therapy for chronic hypertension in pregnancy, rather than the previously recommended threshold of 160/110.

Severe Hypertension

During pregnancy, a BP ≥170/110 mm Hg is considered a medical emergency and requires immediate hospitalization.

Therapy can be initiated with intravenous labetalol, CCBs, or oral methyldopa. Intravenous hydralazine can be used, but it is not currently available in India. Intravenous sodium nitroprusside is contraindicated due to the risk of fetal cyanide toxicity. Intravenous nitroglycerine is the drug of choice in cases of severe hypertension with pulmonary edema.

Intravenous magnesium sulfate is the drug of choice both for the prevention and treatment of seizures (eclampsia).

In some cases of eclampsia, antihypertensive treatment fails to control the BP, and the only means to control it would be to induce delivery.

For women with hypertension during pregnancy, BP should be measured within 6 hours of delivery and, if possible, daily for at least one week after discharge from the hospital. Postpartum hypertension is common in the first week after delivery and is associated with prolonged hospitalization.[6]

Hypertension in Young Adults, Elderly, and Isolated Systolic Hypertension

Hypertension in Young Adults

In this guideline, young adults are defined as those aged 18–40 years. An unhealthy lifestyle, gender, obesity, and socioeconomic variables influence early hypertension onset. Systolic and diastolic hypertension and isolated diastolic hypertension are related with higher CVD risk in the young.[5]

Isolated Systolic Hypertension in Young Adults

Arterial stiffness should be evaluated as it distinguishes isolated systolic hypertension from systolic-diastolic hypertension and isolated diastolic hypertension.[5]

Isolated Diastolic Hypertension in Young Adults

Characterized by systolic BP <140 mm Hg and diastolic BP ≥90 mm Hg. Isolated diastolic hypertension is common in younger adults with obesity or metabolic disorders. The CVD risk in these patients is low (<10% over 10 years), so initiation of BP-lowering medication is unclear, particularly among patients with baseline systolic BP already within the target of 120–129 mm Hg. Irrespective, people with isolated diastolic hypertension should be followed up, since they are at a higher risk of developing systolic hypertension.[5]

Secondary Hypertension in Young Adults

More prevalent in early (15–30%) than in later-onset hypertension. The major causes include drug-induced hypertension (e.g., estrogen-progesterone oral contraceptives, cold medicine) and primary aldosteronism. The usage of recreational drugs/substances, as well as supplements and energy drinks, should be checked. Among obese young people, primary hypertension is more likely, although OSA should also be addressed in this scenario.[5]

Measurement and Control of Blood Pressure in Young Adults: Out-of-office BP measurement is indicated in young adults for verifying diagnosis, as the white-coat effect is common. However, HMOD evaluation may be useful in patients aged <40 years to stratify those with high-normal BP into a higher risk category.[5]

Hypertension in the Elderly

The prevalence of hypertension increases with age. The proportion of senior people in India is predicted to double to over 20% of the total population by 2050, as per the 2023

India Aging Report by the United Nations Population Fund, India (UNFPA).[198] In the older population, systolic hypertension is the most common type of hypertension. The target for BP control is <140/80 mm Hg for people aged 55–79 years. However, for persons aged >80 years, a systolic BP of 140–145 mm Hg is adequate.[5]

Precautions in Measurement

BP should be recorded with care in senior persons as some older patients may show falsely high values due to excessive vascular stiffness. Also, as elderly individuals are more likely to experience orthostatic hypotension, one should test the BP in supine, sitting and standing postures.[6]

Management

Lifestyle adjustments help control hypertension in elderly. Losing weight and reducing the salt intake can lower and even eliminate the need for BP-lowering medications in elderly (Trial of Nonpharmacological Interventions in the Elderly–TONE).[5,6]

Pharmacological Treatment

BP should be reduced gradually in senior hypertensive patients with no more than an initial 25% fall, even in cases necessitating a quick reduction in BP using drugs. Long-acting dihydropyridine CCBs, notably amlodipine, are considered the treatment of choice in these patients as they are successful in lowering mortality and morbidity. Low-dose hydrochlorothiazide, chlorthalidone (6.25 to 12.5 mg per day), or indapamide (1.25–2.5 mg per day) can also be prescribed. In India, diuretics should be used with caution due to the increased risk of hyponatremia, especially in the summer months. Where indicated, they might be used with ACE inhibitors or ARBs.[6] Bilateral atherosclerotic renovascular disease in the elderly must be kept in mind while starting treatment with ACE inhibitors or ARBs.

The HYVET trial and HYVET Extension both offer evidence regarding the effectiveness of BP reduction in the octogenarians and the necessity for early and maintained antihypertensive therapy even in this patient group.[6]

Isolated Systolic Hypertension

Defined as systolic BP of ≥140 mm Hg with a diastolic BP of <90 mm Hg. Isolated systolic hypertension is uncommon in younger patients but is the most common kind of hypertension in elderly patients; >80% of untreated patients with hypertension aged >60 years have isolated systolic hypertension.[5]

Risk Factors

Systolic BP increases with age in men and women until the eighth decade of life, whereas diastolic BP gradually increases up until the fifth or sixth decade of life, after which it either plateaus or decreases. As a result, the pulse pressure gradually widens from middle age onwards. These BP alterations are attributed to an increase in aortic stiffness with aging.[5]

Since older patients often have isolated systolic hypertension and systolic BP drives the risk of CVD events, the management of isolated systolic hypertension is in line with that of routine antihypertensive practices. Solitary systolic hypertension in young patients, although uncommon, is often effectively treated with lifestyle adjustment and long-acting β-blockers.[6] In elderly patients, β-blockers should be avoided in cases of isolated systolic hypertension or more generally in cases of arterial stiffness, as they increase stroke volume (given the lower heart rate).[5]

Isolated Diastolic Hypertension

Isolated diastolic hypertension is defined as a systolic BP of <140 mm Hg with a diastolic BP of ≥90 mm Hg. The isolated diastolic hypertension is more commonly seen in younger adults, particularly with obesity or other metabolic derangements.

Patients with isolated diastolic hypertension should be followed up, as they are at an increased risk for systolic hypertension. After achieving a target systolic BP of 120–129 mm Hg, there is little evidence to justify intensifying anti-hypertensive drugs to achieve a diastolic BP < 70 mm Hg if the systolic BP is < 120 mm Hg.[5]

Orthostatic Hypotension

Orthostatic hypotension (OH), often referred to as postural hypotension, is a condition marked by a pronounced drop in BP when an individual moves from a seated or lying position to a standing position. This sudden change in posture can lead to symptoms such as dizziness, light-headedness, and even fainting (syncope) in severe cases. Clinically, OH is defined by a decrease of at least 20 mm Hg in systolic BP or a drop of 10 mm Hg in diastolic BP within 3 minutes of standing.[199] A condition that disproportionately affects older adults and those with neurological disorders, OH has been linked to higher rates of morbidity and mortality.

Understanding the Prevalence and Impact of Orthostatic Hypotension

Orthostatic hypotension affects approximately 6% of the general adult population and is even more prevalent in those over 65 years of age. Studies indicate that nearly 18% of elderly individuals may experience OH, particularly those with neurodegenerative disorders like Parkinson's disease, multiple system atrophy, and autonomic failure.[199,200] OH is not just an incidental finding but a condition that can compromise daily functioning, impacting the quality of life, in severe cases, it can lead to falls and fractures, especially in older adults. For healthcare providers, recognizing OH is essential due to its association with increased morbidity, which can complicate the management of coexisting conditions such as CVD, diabetes, and hypertension.

Mechanisms and Risk Factors

Orthostatic hypotension occurs when the body fails to properly regulate BP in response to changes in position. Under normal circumstances, standing upright prompts a reflex increase in heart rate and vascular tone, which helps maintain BP. In patients with OH, however, this response is blunted, resulting in a BP drop. Several factors contribute to this impaired response, including autonomic dysfunction, volume depletion, and certain medications.[201]

Elderly individuals, especially those with existing health conditions, are at higher risk of developing OH. The risk is further elevated among individuals taking medications such as antihypertensives, diuretics, α-blockers, vasodilators, ACE inhibitors, and certain antidepressants, which can all exacerbate BP reductions.[6] Neurological disorders and dehydration also play a significant role, making OH a multifactorial condition that requires a comprehensive approach to management.

Recognizing the Symptoms of Orthostatic Hypotension

The symptoms of OH typically occur within minutes of standing and may vary in intensity based on the severity of the BP drop. Common symptoms include:

- Dizziness and light-headedness: Patients often feel dizzy or lightheaded upon standing.
- Blurred vision: A sudden loss of clarity in vision can occur due to the reduced blood flow to the brain.
- Weakness and fatigue: Persistent episodes can cause overall body weakness and fatigue.
- Nausea: Some patients may experience gastrointestinal discomfort.
- Fainting (Syncope): In more severe cases, the sudden decrease in BP can lead to syncope.

These symptoms are not only distressing but can also lead to falls and injuries, emphasizing the need for prompt management.

Diagnostic Criteria and Clinical Evaluation

The diagnosis of OH typically involves measuring BP in the supine, seated, and standing positions, with measurements taken immediately after standing and then repeated at 1 and 3 minutes. A decrease of 20 mm Hg in systolic BP or 10 mm Hg in diastolic BP confirms the diagnosis. In some cases, a tilt table test may be employed, particularly for individuals whose symptoms are inconsistent or difficult to reproduce in a clinical setting.

Apart from BP measurements, a thorough patient history and physical examination are critical in diagnosing OH. Identifying potential triggers, such as recent medication changes or underlying health conditions, is essential for understanding the root causes and formulating an effective management plan.

Management Strategies for Orthostatic Hypotension

Nonpharmacological Approaches

Nonpharmacological strategies form the cornerstone of OH management and often serve as the first-line approach. They focus on lifestyle changes and physical measures that help stabilize BP without relying on medication.

- *Patient education and lifestyle modifications:* Educating patients on OH and advising them on avoiding sudden postural changes is vital. Patients should be encouraged to rise slowly from seated or lying positions to allow their bodies time to adjust. Adequate hydration is another key element, as it helps maintain blood volume and supports BP stability. Ensuring patients understand the importance of these habits can significantly reduce the frequency and severity of OH episodes.[200,201]
- *Dietary adjustments:* Increasing both salt and fluid intake can be beneficial, as these measures help expand blood volume, potentially reducing the symptoms of OH. For those without contraindications, salt tablets or higher-salt foods may be recommended to help retain fluid and improve blood pressure control.[201]
- *Physical countermeasures*: Simple maneuvers like crossing the legs, performing leg exercises, and squatting can improve venous return to the heart, thereby increasing BP. Physical countermeasures are particularly useful for those who experience symptoms in situations where medication may not be practical, such as during daily activities or work.[202]
- *Postural aids:* Compression garments, such as thigh-high compression stockings or abdominal binders, can prevent blood from pooling in the lower extremities. By supporting circulation, these aids can help stabilize the BP upon standing and reduce OH symptoms. Such interventions are particularly beneficial for individuals who remain symptomatic despite lifestyle modifications and other non-pharmacological measures.[201]

Pharmacological Treatments

When nonpharmacological measures are insufficient, pharmacological treatment may be introduced. Antihypertensive drugs that worsen OH should be discontinued and switched to alternate drugs. Certain medications aim to support BP stability and can be chosen based on individual patient needs and risk factors.

First-line medications: The most commonly used drugs for OH are midodrine and fludrocortisone. Midodrine works by increasing vascular tone, thus preventing BP from dropping upon standing. Fludrocortisone, a synthetic corticosteroid, helps retain sodium and water, increasing blood volume and BP. These medications have demonstrated efficacy in clinical trials and are generally well-tolerated.[6,201] Clinicians should also be aware of supine hypertension, a condition where BP rises excessively when lying down, which can be particularly problematic in OH patients.[199,203]

Alternative medications: For patients who do not respond to first-line treatments, additional medications such as pyridostigmine, atomoxetine, and droxidopa may be considered.[200]

Hypertension with Obesity and Metabolic Syndrome

Prevalence and Impact of Obesity and Metabolic Syndrome

The National Family Health Survey (NFHS, 2019–21) of India defined individuals with a BMI >25 kg/m^2 as overweight and those with a BMI >30 kg/m^2 as obese.[204] In Asians, the BMI cut-offs for overweight (>23.0 kg/m^2) and obesity (>25.0 kg/m^2) are lower than the WHO criteria. These provisional recommendations will need to be revised in the light of further validation studies and clinical experience (Table 30).[6]

Epidemiological studies have consistently shown a tight correlation between body weight and blood pressure, with 70% of hypertension in men and 60% in women being directly attributable to excess adiposity. Essential hypertension is very frequently associated with a decrease in insulin sensitivity. This insulin resistance is very often associated with dyslipidemia, obesity, hypertension, and impaired glucose tolerance, a cluster termed the "metabolic syndrome or the insulin resistance syndrome".[6]

Truncal obesity is more prevalent in the Indian population.[6] Even in cases of obesity without metabolic syndrome, there is a 45% greater relative risk of CVD events.[204] Abdominal obesity is related to salt retention, endothelial dysfunction, microalbuminuria, LVH, and increased markers of inflammation.[204]

The National Family Health Survey (NFHS, 2019–21) of India assessed abdominal obesity based on waist circumference. The prevalence of abdominal obesity was found to be high in India. Overall, 40% of women and 12% of men were found to be abdominally obese. However, only 23% of the women were deemed obese based on BMI. This indicates that some women who have a healthy BMI also happen to have abdominal obesity. Abdominal or central obesity is defined as having a waist circumference of more than 80 cm in women and more than 94 cm in men. It is a strong predictor of CVDs, type-2 diabetes, and other metabolic disorders.[204]

Lifestyle modification (diet, exercise) is the cornerstone for the management of hypertension in obese patients. According to associated metabolic syndromes, specific drugs can be prescribed to lower BP without exacerbating the metabolic abnormalities that accompany hypertension in obese individuals.[205]

On the basis of their favorable metabolic profiles, ACE inhibitors, ARBs, CCBs, and α-blockers appear to be effective at decreasing BP without worsening the metabolic abnormalities that accompany hypertension in obese patients. ACE inhibitors, low-dose diuretics, and nondihydropyridine CCBs should be the drugs of first choice in this setting. Notably, α -blockers demonstrate particular advantages in individuals with dyslipidemia or glucose intolerance and may be considered as add-on agents.[6]

Additionally, therapies targeting weight loss such as GLP-1 receptor agonists (semaglutide)[206] or GIP/GLP-1 receptor agonists (tirzapetide),[207] have shown efficacy in reducing BP in initial studies. Bariatric surgery can also be considered in selected patients.[208]

Table 30: Diagnostic criteria for metabolic syndrome proposed by various authoritative professional organisations[209]

Component	*Name of Professional Body*	
	WHO	NCEP–ATP–III
Essential components	Indicators of insulin resistance[a]	NIL
Other components (other than essential)		
Insulin resistance or hyperinsulinemia	Essential criteria as above	NA
Waist circumference (WC)[b]	NA	≥102 in males; ≥88 in females
Waist: Hip Ratio (WHR)	≥0.90 in males; ≥0.85 in females c	NA
Serum triglycerides (mg/dL)[d]	≥150	≥150
Serum HDL-C[d]	<35 (males); <39 (females)	<40 (males); <50 (females)
Systolic blood pressure (SBP)/diastolic blood pressure (DBP) mm Hg[d,e]	≥140/90	≥130/85
Fasting plasma glucose (mg/dL)[d,f]	Essential criteria as above	≥100
Microalbuminuria	Urinary albumin >20 µg/min or albumin: creatinine ratio ≥30 mg/g	NA
Final diagnostic criteria	Essential criteria as above (IR/IFG/IGT/T2DM) plus any two of the other	Any three of the five criteria (no essential criteria)

[a]Insulin resistance (IR) as evidenced by clamp studies, or presence of impaired glucose tolerance/impaired fasting glucose/T2DM; [b]WC, waist circumference in centimeters; [c]If Body Mass Index (BMI) is ≥30 kg/sq meters, then WHR need not be measured as per WHO criteria; [d]In addition to the cut-off for raised triglycerides, lowered HDL-C, raised BP or increased fasting glucose, existing drug treatment for these abnormalities will also be considered as an inclusion criterion; [e]Rise in either systolic blood pressure/diastolic blood pressure in mm Hg would be a criterion; [f]It may be mentioned that the World Health Organization (WHO) still maintains that the cut-off for impaired fasting glucose should be > 110 mg/dL and not at >100 mg/dL as has been recommended by several other professional bodies. This decision was based on concerns about the significant increase in impaired fasting glucose/impaired fasting hyperglycemia (IFG) prevalence, which would occur with lowering the cut-point and the impact on individuals and health systems.

Hypertension with Obstructive Sleep Apnea

Prevalence and Impact of Obstructive Sleep Apnea

OSA is characterized by a stop-and-start breathing pattern with full and partial obstructions of the upper airway, leading to intermittent hypoxemia, autonomic variability, and disrupted sleep. Around 34% of middle-aged men and 17% of middle-aged women fulfill diagnostic criteria for OSA, though far more are frequently underdiagnosed and inadequately managed. The prevalence of OSA ranges from 40% to 80% among individuals with hypertension, heart failure, CAD, pulmonary hypertension, AF, and stroke. 30% to 50% of hypertensive patients have comorbid OSA, and the proportion is even higher (80%) in those with resistant hypertension.[209] The pooled prevalence of OSA (apnea/hypopnea index–AHI ≥5 events/hour) is 11% overall, 13% in men, and 5% in women.[210] OSA screening is recommended in patients exhibiting resistant/poorly managed hypertension, pulmonary hypertension, and recurrent AF after either cardioversion or ablation. In patients with comorbid hypertension and OSA, not all hypertension is attributed to OSA, hence therapy of OSA should not always be expected to consistently decrease BP.[211]

Poor BP control is strongly associated with OSA, especially in those patients with an apnea/hypopnea index of at least 30 events per hour.[212] The awareness about OSA remains dismally low in India.

Recognizing the Symptoms of Obstructive Sleep Apnea

Restless/intermittent sleep, recurrent awakenings, daytime somnolence, fatigue, impaired concentration, snoring, increased neck circumference, obesity, gasping during the night, AF, and non-dipping or reverse dipping pattern on 24-hour ambulatory BP monitoring are symptoms of OSA.[5]

Diagnostic Criteria and Clinical Evaluation of Obstructive Sleep Apnea

A sleep study (polysomnography) confirms the diagnosis by measuring the AHI. OSA is mild if AHI is <15, moderate if AHI is 15 to 30, and severe if AHI is >30.[5] Nowadays, the increased availability of wearable devices and remote monitoring technologies offers extensive prospects for screening for the prevalence of sleep-disordered breathing.[210]

Management Strategies for Obstructive Sleep Apnea

For mild OSA with AHI <15, weight loss and sleep hygiene guidance can be provided. For moderate OSA with an AHI of 15 to 30 and severe OSA with AHI > 30, continuous positive airway pressure (CPAP) is needed.[5]

Nonpharmacological Approaches

- The impact of CPAP therapy to reduce BP among hypertensive patients with OSA have been unsatisfactory and inconsistent. A meta-analysis revealed reductions of 2–3 mm Hg BP. Hence, adjuvant drug therapy is required.[210,212]
- CPAP enables the reduction of both daytime and night-time BP.[6]
- Oral appliance therapies like soft-palate lifters, tongue-retaining devices and mandibular advancement devices can provide similar BP reductions as CPAP.[5, 210]

Pharmacological Treatments

There are no specific drugs for OSA treatment.[5] ARBs, certain β-blockers, central α-agonists such as clonidine or guanfacine and longer-acting drugs with similar action can improve BP control during bedtime.[212]

Surgical Treatments

If CPAP is not tolerated, the source of upper airway obstruction should be detected by an ear, nose, and throat assessment with drug-induced sleep endoscopy. Subsequently, corrective surgery can be performed to open the airway.[5] Uvulopalatopharyngoplasty may be beneficial in selected patients, with considerable decreases of 4–9 mm Hg reported at 6 and 24 months following surgery in a small randomized controlled trial.[210]

Hypertension and Malignancy

Hypertension is a frequent long-term sequela of various cancer treatments, including both chemotherapy and targeted therapies. Arterial hypertension is notably prevalent among cancer patients, with

its incidence rising in parallel to the aging population in developed nations. Hypertension is the most frequent adverse effect of anti-vascular endothelial growth factor (VEGF) therapy. The overall incidence of hypertension during cancer therapy ranges from 20% to 44%, with high-grade hypertension occurring in 6–17% of cases, particularly during active treatment. The prevalence of hypertension is influenced by several factors, including the patient's age, pre-existing hypertension or CVD, the type of malignancy (renal vs. non-renal), the specific cancer therapy and its dosage, the chemotherapy regimen, and any concomitant medications.[213]

Management

There is limited evidence to support a specific antihypertensive strategy for managing hypertension induced by anticancer therapies. First-line treatment should include an ARB or ACE inhibitor, a dihydropyridine CCB or a thiazide/thiazide-like diuretic. Patients with proteinuria should be managed with an ARB or ACE inhibitor. Diuretics should be avoided in patients at high risk for volume depletion. For resistant hypertension, MRAs are recommended as the initial treatment unless contraindicated, such as in cases of hyperkalemia. Importantly, β-Blockers should not be used as first-line agents and should be reserved for patients with specific indications (e.g., AF, recent MI, HFrEF) or those with contraindications to the above agents. Non-dihydropyridine CCBs (e.g., diltiazem, verapamil) should be used cautiously due to potential interactions with anticancer therapies metabolized by the P-glycoprotein and cytochrome P450 3A4 enzymes.[214]

Patients should be counseled on lifestyle changes and evaluated for comorbidities, and concomitant therapies should be evaluated to manage hypertension during cancer treatment.[214]

Hypertension in Postoperative Patients

Postoperative hypertension is characterized by an acute, transient elevation in BP occurring within 30 to 90 minutes post-surgery and typically resolving within 4–8 hours. It is defined by a systolic BP exceeding 160 mm Hg or a diastolic BP over 90 mm Hg. This hypertensive response is primarily driven by increased systemic vascular resistance, resulting from reflexive changes in humoral factors such as elevated catecholamines, renin, and serotonin, along with impaired baroreceptor function and altered carotid reflexes.[215]

Acute postoperative hypertension (APH) can lead to several serious complications, including hemorrhagic stroke, cerebral ischemia, hypertensive encephalopathy, myocardial ischemia, MI, cardiac arrhythmias, congestive heart failure with pulmonary edema, failure of vascular anastomoses, and surgical site bleeding.[216]

Management

The preferred pharmacologic agents for treating APH should exhibit a rapid onset and a short to intermediate duration of action, with proven efficacy and safety. Sodium nitroprusside, nitroglycerine, labetalol, and nicardipine are the agents of choice in most clinical scenarios. Selection of the appropriate agent should be guided by the specific clinical context, patient characteristics, care setting, and clinician expertise. Sublingual nifedipine is not recommended.[216]

ACE inhibitors are also utilized in managing postoperative hypertension. In patients with hypertension following neurosurgical procedures, direct-acting vasodilators should be avoided due to the potential to exacerbate intracranial pressure elevations. In these cases, β-adrenergic receptor antagonists and ACE inhibitors are the preferred treatment options.[216]

Resistant Hypertension

Resistant hypertension is defined as the failure to reach target BP in patients who are adhering to maximally tolerated doses of an appropriate 3-drug regimen of different classes that includes a diuretic. This condition poses significant challenges for both patients and healthcare providers, as it increases the risk of cardiovascular events such as heart attacks, strokes, and kidney failure.[217] The causes of resistant hypertension are shown in Table 31.

Clinical Approach to Resistant Hypertension

About 12.2% of hypertensive patients have Resistant Hypertension. Ambulatory blood pressure monitoring should be done in these patients in order to classify them as follows:[5]

- True resistant hypertensives (62.5%).
- Pseudo or white-coat resistant hypertension (37.5%).

True resistant hypertensive patients are more commonly men, of younger age, with a longer duration of hypertension, smokers, diabetics, HMOD (including left ventricular hypertrophy, impaired renal function, and microalbuminuria), and overall, a worse cardiovascular risk profile.

Therefore, it is necessary to use ambulatory blood pressure monitoring for a correct diagnosis and management of true resistant hypertension.

Table 31 gives causes of resistant hypertension. These causes can be readily identified and treated.

Table 31: Causes of resistant hypertension[5,6,217]

Volume overload	Excess sodium intake Volume retention from kidney disease
Drug	Inadequate doses Inappropriate combinations Nonsteroidal anti-inflammatory drugs and cyclooxygenase two inhibitors Cocaine, amphetamines, and other illicit drugs Cyclosporine and tacrolimus Tobacco Selected over-the-counter dietary supplements and medicines (e.g., licorice and cough syrups)
Associated conditions	Obesity Excess alcohol intake
Secondary causes of hypertension	Chronic kidney disease Coarctation of the aorta Nonspecific aortoarteritis Cushing syndrome and other glucocorticoid excess states, including chronic steroid therapy Obstructive uropathy Pheochromocytoma Primary aldosteronism and other mineralocorticoid excess states Renovascular hypertension Obstructive sleep apnea syndrome Thyroid or parathyroid disease

Management of Resistant Hypertension

- Most patients with resistant hypertension need to be referred to specialized hypertension clinics after confirmation of the level of compliance.
- Aggressive salt restriction should be instituted along with other lifestyle changes. Drugs interfering with action of antihypertensive agents should be eliminated.
- Additionally, a detailed workup for secondary hypertension should be carried out.
- In case no causes of secondary hypertension are detected, multiple drugs in high dosages should be started. Attention should be paid to the timing of medications and compliance with therapy.
- After increasing to maximally tolerated doses of ACEI/ARB, CCB, and Thiazide diuretic and making sure of compliance, an MRA (Spironolactone/Eplerenone) should be added to control the BP (Step 4 in Fig. 14).[6]
- In case BP is still not controlled, second-line antihypertensive drugs can be added, including alpha blockers, centrally acting agents, or direct vasodilators. Other drugs that can be considered include ARNI or SGLT2 inhibitors. (Step 5 in Fig. 14)
- Intervention-based treatment modalities such as renal sympathetic denervation therapy should also be considered. Other interventional-based therapies, such as Carotid Baroreceptor Stimulation therapy are being evaluated.[6]

Technology and Hypertension

Technology in Hypertension Management

Hypertension continues to be a major public health concern worldwide, with a substantial proportion of individuals either undiagnosed or inadequately controlled. The rapid evolution of digital health technologies, such as self-monitoring (home monitoring), telemonitoring, and virtual clinics, offers innovative opportunities to strengthen hypertension management and patient engagement. The 2024 ESC Guidelines for managing elevated BP emphasize multidisciplinary approaches, including task-shifting and the self-measurement of BP, as strategies to improve BP control. These advancements aim to reduce the dependence on in-person visits, improved follow-up care, and ultimately lower the risk of severe CV events. Although enhanced self-monitoring shows promise, evidence for its superiority over standard methods is limited, highlighting the need for clinical validation.[5,218]

Home blood pressure monitoring/self-monitoring: Regular self-monitoring of BP using home devices is emphasized as a strongly encouraged for achieving better BP control. This approach empowers patients to actively participate in their health management, enhances their awareness of their condition, and facilitates regular communication of BP readings to healthcare providers.[5,218]

Digital communication tools: Web-based communication systems between clinicians and patients are increasingly used in primary care settings. These platforms allow electronic sharing of home BP readings and related health data, thereby improving the management of hypertension.[5]

Digital monitoring tools: Technological advancements have enabled continuous and more precise BP tracking. Connected BP monitors, patient-facing mobile applications, and wearable devices provide real-time data that can support prompt clinical interventions. By reducing the white-coat effect and enabling out-of-office measurement, these tools may enhance accuracy. Applications and wearable devices facilitate remote monitoring, reducing clinic visits and improving treatment adherence. Digital health presents a viable mechanism for delivering hypertension care that is more scalable, comprehensive, and efficient, thereby surpassing conventional office-based care models in terms of BP regulation and patient engagement. However, widespread implementation requires careful validation and standardization. These technologies are key to addressing gaps in traditional hypertension management, promoting better outcomes, and improving healthcare efficiency.[219]

Smartphone applications: The use of mobile health applications on smartphones enables patients to track their BP and health metrics conveniently. These applications can often be synchronized with monitoring devices, providing a comprehensive overview of the patient's health.[219] While current evidence suggests that these applications may not significantly outperform structured self-monitoring alone, they represent meaningful progress in patient engagement, longitudinal data collection, and remote disease tracking.[5]

Cuff-less ambulatory blood pressure monitoring devices: These devices represent a significant advancement in the continuous monitoring of BP. These devices are designed to offer a non-intrusive alternative to traditional cuff-based systems, enhancing patient compliance and comfort. Commonly, they utilize ECG and photoplethysmogram (PPG) signals, or a combination of both, to estimate BP levels. Some devices have integrated machine learning algorithms and neural networks to improve measurement accuracy and predictive capabilities.[218]

These sensors can be incorporated into various wearable technologies, such as wristwatches, T-shirts, heart rate belts, eyeglass frames, or devices positioned behind the ears. The collected data are often transmitted to smartphone applications, enabling real-time monitoring and analysis.[218]

The primary advantages of cuff-less ambulatory BP systems include convenience of continuous, nonintrusive monitoring, portability, and comfort, which make it ideal for everyday use. Nevertheless, concerns remain regarding measurement consistency, calibration requirements, and limited large-scale validation studies. As such, their routine clinical application remains under evaluation.[218]

- *Virtual clinics*: Virtual clinics leverage these technologies to provide remote consultations and hypertension management. They can enhance access to care, especially for patients who may have logistical barriers to in-person visits.[218]
- *Artificial intelligence (AI)*: AI-assisted management tools are being explored to analyze BP data and provide personalized treatment recommendations. This can enhance the decision-making process for healthcare providers. These systems may augment clinician judgment by identifying trends within large datasets.[218]
- *Facilitating medication adherence*: Technology can help in medication management by providing reminders and tracking adherence. The use of long-acting drugs and single-pill combinations to simplify regimens can be supported by digital tools to enhance adherence.[5] At present, there are intelligent pill boxes supported by AI that can remind the patient, in case they forget to take their medicines.

Telemonitoring

Healthcare professionals can remotely check patients' BP readings via telemonitoring. This technology can facilitate timely interventions and adjustments to treatment plans based on real-time data.[219] Telemonitoring is a broader telehealth strategy component that includes various services delivered through technology, such as phone reviews, video consultations, and web-based communication. This comprehensive approach can enhance patient education, medication adherence,

and the overall management of hypertension. Studies indicate that patients generally find these programs acceptable, which can lead to improved BP control and treatment intensification.[220]

Key Benefits of Telemonitoring[220]

- Improved BP control through continuous BP oversight.
- Facilitates timely treatment intensification and optimization.
- Reduces clinic visit frequency and the need for in-person consultations.
- Enhances quality of life by flexible and effective management of BP.
- Improved medication adherence.
- Improves drug safety by monitoring potential adverse effects.
- More efficient healthcare resource utilization and thereby reduced management costs.
- Improves outcomes by reducing the risk of hospitalization or adverse cardiovascular events.

In summary, technology aids in the treatment and management of hypertension through home monitoring, digital communication, enhanced self-monitoring devices, multidisciplinary care, and improved medication adherence strategies. These digital technologies represent a shift towards more patient-centered care in hypertension management, aiming to improve overall health outcomes.

Role of Artificial Intelligence in Hypertension Management[221]

- *Predictive modeling*: AI can predict the probability of developing hypertension by aggregating various data sources, including genetic, medical, and lifestyle factors. Predictive modeling provides the opportunity for early intervention that can potentially avoid or delay the onset of hypertension.
- *Improved diagnosis*: AI helps diagnose hypertension by processing patient data more effectively than traditional methods. It can help diagnose secondary causes of hypertension, which is important for effective treatment. AI algorithms can also improve the accuracy of BP measurements through innovative techniques like PPG
- *Monitoring and compliance*: AI technologies can facilitate the continuous monitoring of BP through wearable devices, promoting patient awareness and adherence to treatment. Such real-time data collection can lead to timely adjustments in therapy based on individual responses.
- *Improving treatment strategies*: Machine learning algorithms can analyze real-world data to identify patterns and trends that inform treatment strategies. This capability is particularly useful in evaluating the effectiveness of different drug combinations and optimizing therapy.
- *Limitations of AI*: Even though AI brings a lot of benefits, there are still many challenges. The problems include overfitting, data biases, and the "black box" problem of some algorithms, which can be detrimental to hypertension management, making the outcomes unreliable and non-interpretable.

In conclusion, AI has the potential to revolutionize hypertension management by providing personalized treatment options, enhancing diagnostic accuracy, and improving patient monitoring and compliance. Its integration into clinical practice could lead to more effective and efficient care for individuals with hypertension.

Role of Social Media in Hypertension Management and Awareness[222]

Social media plays a pivotal role in the management and awareness of hypertension, offering potential benefits in improving patient lifestyles and enhancing pharmacological adherence over traditional methods. Its impact is generated through increased awareness, bidirectional communication, and the involvement of qualified healthcare professionals. However, the use of social media also carries risks, including the spread of misinformation and potential emotional effects that may elevate BP. Integrating social media into health programs is advocated to optimize hypertension management and promote better health outcomes.

- *Information dissemination*: Social media serves as a powerful platform for distributing health-related information, breaking down barriers related to race, cost, and geography. More than 58% of hypertension patients have accessed websites for medical information, highlighting the potential of social media to raise awareness about hypertension management.
- *Community engagement*: Social media facilitates the creation of community groups focused on hypertension, where objectives include raising awareness (60%), supporting patients or caregivers (11%), and sharing experiences (10%). This community aspect can enhance patient support and knowledge sharing.
- *Increased participation in programs*: Campaigns, such as Measure Your Blood Pressure (MYP), have shown that social media advertising significantly increases participation in hypertension programs compared to traditional methods. For instance, MYP reached 80,000 users on Facebook, demonstrating the platform's effectiveness in engaging a larger audience.
- *Motivation and lifestyle changes*: Social media-based health promotion can improve motivation and attitudes towards chronic disease treatment, which is crucial for better outcomes in hypertension management. The interaction on these platforms can lead to lifestyle modifications and better adherence to pharmacological treatments.
- *Bidirectional communication*: The effectiveness of social media in hypertension management is enhanced by bidirectional communication between patients and healthcare providers. This interaction can improve the quality of treatment and adherence to health guidelines.
- *Challenges and risks*: Despite its benefits, social media also poses risks, such as the spread of misinformation and misunderstandings about health information. The presence of experts in hypertension-related groups is minimal, which can lead to the rapid spread of hoaxes.
- *Screen time concerns*: Increased screen time associated with social media use may also contribute to higher BP due to sedentary lifestyle patterns and emotional stress.

Overall, social media enhances hypertension management through information sharing, community engagement, and improved adherence. While it promotes awareness and lifestyle changes, challenges like misinformation and screen time risks must be addressed. Structured integration can optimize the benefits of this tool for better outcomes.

References

1. National High Blood Pressure Education Program. The seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Bethesda (MD): National Heart, Lung, and Blood Institute (US); 2004 Aug. Blood pressure and cardiovascular risk. [online] Available from: https://www.ncbi.nlm.nih.gov/books/NBK9634/
2. Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002;360(9349):1903–1913.
3. Mourad JJ. The evolution of systolic blood pressure as a strong predictor of cardiovascular risk and the effectiveness of fixed-dose ARB/CCB combinations in lowering levels of this preferential target. Vasc Health Risk Manag 2008;4(6):1315–1325.
4. Jones DW, Ferdinand KC, Taler SJ, et al. 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM guideline for the prevention, detection, evaluation and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2025;152(11):e114–e218.
5. McEvoy JW, McCarthy CP, Bruno RM, et al. 2024 ESC guidelines for the management of elevated blood pressure and hypertension: developed by the task force on the management of elevated blood pressure and hypertension of the European Society of Cardiology (ESC) and endorsed by the European Society of Endocrinology (ESE) and the European Stroke Organisation (ESO). Eur Heart J 2024;45(38):3912–4018.
6. Shah SN, Munjal YP, Kamath SA, et al. Indian guidelines on hypertension-IV (2019). J Hum Hypertens 2020;34(11):745–758.
7. Vasan RS, Song RJ, Xanthakis V, et al. Hypertension-mediated organ damage: prevalence, correlates, and prognosis in the community. Hypertension 2022;79(3):505–515.
8. Indian guidelines management of hypertension 2001. Hypertension India 2001;15:1–34.
9. Williams B, Poulter NR, Brown MJ, et al. Guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004—BHS IV. J Hum Hypertens 2004;18(3):139–185.
10. Zheng R, Xu Y, Li M, et al. Examining the linear association between blood pressure levels and cardiovascular diseases in the absence of major risk factors in China. Circ Cardiovasc Qual Outcomes 2022;15(9):e008774.
11. Schillaci G, Pucci G. The dynamic relationship between systolic and diastolic blood pressure: yet another marker of vascular aging? Hypertens Res 2010;33(7):659–661.
12. Vidt DG, Basile JN. Hypertension curriculum review. The importance of systolic blood pressure elevation in elderly persons. J Clin Hypertens (Greenwich) 2004;6(8):461–465.
13. Mancia G, Bombelli M, Lanzarotti A, et al. Systolic vs diastolic blood pressure control in the hypertensive patients of the PAMELA population. Arch Intern Med 2002;162(5):582–586.
14. Franklin SS. Systolic blood pressure: it's time to take control. Am J Hypertens 2004;17(S3):49S–54S.
15. SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med 2015;373:2103–2116.
16. World Health Organization. Epidemiology of hypertension. Geneva: WHO; 2023.
17. Amrin S, Borah P. Hypertension in India: an insight into the NFHS-5 data. J Pharm Negat Results 2022;13(Spec Issue 8):3552–3554.
18. Prabhakaran D, Jeemon P, Sharma M, et al. The changing patterns of cardiovascular diseases and their risk factors in the states of India: the Global Burden of Disease Study 1990–2016. Lancet Glob Health 2018;6(12):e1339–e1351.
19. World Health Organization. Global health estimates 2019. Geneva: WHO; 2019.
20. Indian Council of Medical Research. Epidemiology of hypertension. New Delhi: ICMR; 2023.
21. Kostev K, Krieg S, Jacob L. Trends in hypertension and hypertension treatment in primary care in general practices in Germany between 2013 and 2022. Front Cardiovasc Med 2024;11:1390902.
22. Izzo JL Jr, Levy D, Black HR. Importance of systolic blood pressure in older Americans. Hypertension 2000;35(5):1021–1024.
23. Measurement of blood pressure. JAPI 2013;61(Suppl):14–5.
24. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. Eur Heart J 2018;39(33):3021–3104.
25. O'Flynn AM, Madden JM, Russell AJ, et al. Isolated nocturnal hypertension and subclinical target organ damage: a systematic review of the literature. Hypertens Res 2015;38:570–575.
26. Kario K. Morning surge in blood pressure and cardiovascular risk: evidence and perspectives. Hypertension 2010;56(5):765–773.
27. Raza M, Bansod DW. Hypertension in India: a gender-based study of prevalence and associated risk factors. BMC Public Health 2024;24:2681.
28. Officers AL. Diuretic versus α-blocker as first-step antihypertensive therapy: final results from the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). Hypertension 2003;42:239–246.
29. Staessen JA, Fagard R, Thijs L, et al. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. Lancet 1997;350(9080):757–764.
30. SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. JAMA 1991;265(24):3255–3264.
31. Dahlöf B, Sever PS, Poulter NR, et al. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. Lancet 2005;366(9489):895–906.
32. ALLHAT Officers, Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA 2002;288:2981–2997.
33. Kim JK, Crimmins EM. Blood pressure and mortality: joint effect of blood pressure measures. J Clin Cardiol Cardiovasc Ther 2020;2(1).
34. Franklin SS, Larson MG, Khan SA, et al. Does the relation of blood pressure to coronary heart disease risk change with aging? The Framingham Heart Study. Circulation 2001;103(9):1245–1249.
35. Frohlich ED. Treating hypertension—what are we to believe? N Engl J Med 2003;348(7):639–641.
36. Mittal RDJ, Mukherjee A, Saxena BN. Salt consumption pattern in India: an ICMR task force study. New Delhi: Indian Council of Medical Research; 1996.
37. Challa HJ, Ameer MA, Uppaluri KR. DASH diet to stop hypertension. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023.
38. Bao DQ, Mori TA, Burke V, et al. Effects of dietary fish and weight reduction on ambulatory blood pressure in overweight hypertensives. Hypertension 1998;32(4):710–717.
39. Rouse IL, Armstrong BK, Beilin LJ. The relationship of blood pressure to diet and lifestyle in two religious populations. J Hypertens 1983;1(1):65–72.
40. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. N Engl J Med 1997;336(16):1117–1124.
41. Srilakshmi B. Diet in diseases of cardiovascular system. In: Srilakshmi B (Ed). Dietetics, 5th edition. New Delhi: New Age International; 2005. pp. 189–213.
42. Srilakshmi B. Diet in diseases of kidney. In: Srilakshmi B (Ed). Dietetics, 5th edition. New Delhi: New Age International; 2005. pp. 267–291.
43. Whelton PK, Appel LJ, Espeland MA, et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). JAMA 1998;279(11):839–846.
44. Ghadieh AS, Saab B. Evidence for exercise training in the management of hypertension in adults. Can Fam Physician 2015;61(3):233–239.
45. Stamler J, Caggiula AW, Grandits GA. Relation of body mass and alcohol, nutrient, fiber, and caffeine intakes to blood pressure in the special intervention and usual care groups in the Multiple Risk Factor Intervention Trial. Am J Clin Nutr 1997;65(1 Suppl):338S–365S.
46. Yusuf S, Joseph P, Rangarajan S, et al. Modifiable risk factors, cardiovascular disease, and mortality in 155,722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. Lancet 2020;395(10226):795–808.
47. Puddey IB, Parker M, Beiten LJ, et al. Effects of alcohol and caloric restrictions on blood pressure and serum lipids in overweight men. Hypertension 1992;20(4):533–541.
48. Stewart SH, Latham PK, Miller PM, et al. Blood pressure reduction during treatment for alcohol dependence: results from the Combining Medications and Behavioral Interventions for Alcoholism (COMBINE) study. Addiction 2008;103(10):1622–1628.
49. Greenberg G, Hompson S, Brennan PJ. The relationship between smoking and the response to anti-hypertensive treatment in mild hypertensives in the Medical Research Council's trial of treatment. Int J Epidemiol 1987;16(1):225–230.
50. Gupta R, Gurm H, Bartholomew JR. Smokeless tobacco and cardiovascular risk. Arch Intern Med 2004;164(17):1845–1849.
51. United States Public Health Service Office of the Surgeon General. Smoking cessation: a report of the surgeon general. Washington (DC): US Department of Health and Human Services; 2020.
52. Verma N, Rastogi S, Chia YC, et al. Non-pharmacological management of hypertension. J Clin Hypertens (Greenwich) 2021;23(7):1275–1283.
53. Patel C. 12-month follow-up of yoga and bio-feedback in the management of hypertension. Lancet 1975;305(7898):62–64.
54. Sundar S, Agrawal SK, Singh VP, et al. Role of yoga in management of essential hypertension. Acta Cardiol 1984;39(3):203–208.
55. Datey KK. Role of biofeedback training in hypertension and stress. J Postgrad Med 1980;26(1):68–73.
56. Damodaran A, Malathi A, Patil N, et al. Therapeutic potential of yoga practices in modifying cardiovascular risk profile in middle-aged men and women. J Assoc Physicians India 2002;50(5):633–640.
57. Thiyagarajan R, Pal P, Pal GK, et al. Additional benefit of yoga to standard lifestyle modification on blood pressure in prehypertensive subjects: a randomized controlled study. Hypertens Res 2015;38(1):48–55.
58. Calhoun DA, Harding SM. Sleep and hypertension. Chest 2010;138(2):434–443.
59. Roomi MH, Srivastava A, Girdhar N, et al. A study of the correlation between screen time and hypertension among young adults in North India: a cross-sectional analysis. Cureus 2024;16(1).

60. Nang EE, Salim A, Wu Y, et al. Television screen time, but not computer use and reading time, is associated with cardio-metabolic biomarkers in a multiethnic Asian population: a cross-sectional study. Int J Behav Nutr Phys Act 2013;10:1–10.
61. Gavras H, Gavras I. On the JNC V Report: a different point of view. Am J Hypertens 1994;7(3):288–293.
62. Van Kempen E, Casas M, Pershagen G, et al. WHO environmental noise guidelines for the European region: a systematic review on environmental noise and cardiovascular and metabolic effects: a summary. Int J Environ Res Public Health 2018;15(2):379.
63. Münzel T, Sørensen M, Daiber A. Transportation noise pollution and cardiovascular disease. Nat Rev Cardiol 2021;18(9):619–636.
64. Prabhakaran D, Mandal S, Krishna B, et al. Exposure to particulate matter is associated with elevated blood pressure and incident hypertension in urban India. Hypertension 2020;76(4):1289–1298.
65. Stergiou GS, Palatini P, Parati G, et al. 2021 European Society of Hypertension practice guidelines for office and out-of-office blood pressure measurement. J Hypertens 2021;39(7):1293–1302.
66. Goyal A, Aslam N, Kaur S, et al. Factors affecting seasonal changes in blood pressure in North India: a population-based four-seasons study. Indian Heart J 2018;70(3):360–367.
67. Goyal A, Narang K, Ahluwalia G, et al. Seasonal variation in 24-hour blood pressure profile in healthy adults: a prospective observational study. J Hum Hypertens 2019;33(8):626–633.
68. PROGRESS Collaborative Group. Randomized trial of a perindopril-based blood pressure-lowering regimen among 6105 individuals with previous stroke or transient ischemic attack. Lancet 2001;358(9287):1033–1034.
69. Dahlöf B, Devereux RB, Kjeldsen SE, et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomized trial against atenolol. Lancet 2002;359(9311):995–1003.
70. Julius S, Kjeldsen SE, Weber M, et al. Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the VALUE randomized trial. Lancet 2004;363(9426):2022–2031.
71. ONTARGET Investigators. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl. J Med 2008;358(15):1547–1559.
72. Haller H, Ito S, Izzo JL Jr, et al. Olmesartan for the delay or prevention of microalbuminuria in type 2 diabetes. N Engl J Med 2011;364(10):907–917.
73. Hansson L, Hedner T, Lund-Johansen P, et al. Randomized trial of effects of calcium antagonists compared with diuretics and β-blockers on cardiovascular morbidity and mortality in hypertension: the Nordic Diltiazem (NORDIL) study. Lancet 2000;356(9227):359–365.
74. Packer M, O'Connor CM, Ghali JK, et al. Effect of amlodipine on morbidity and mortality in severe chronic heart failure. N Engl J Med 1996;335(15):1107–1114.
75. Roush GC, Holford TR, Guddati AK. Chlorthalidone compared with hydrochlorothiazide in reducing cardiovascular events: systematic review and network meta-analyses. Hypertension 2012;59(6):1110–1117.
76. Brown MJ, Williams B, Morant SV, et al. Effect of amiloride, or amiloride plus hydrochlorothiazide, versus hydrochlorothiazide on glucose tolerance and blood pressure (PATHWAY-3): a parallel-group, double-blind randomized phase 4 trial. Lancet Diabetes Endocrinol 2016;4(2):136–147.
77. Williams B, MacDonald TM, Morant S, et al. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomized, double-blind, crossover trial. Lancet 2015;386(10008):2059–2068.
78. Guidelines Committee. 2003 European Society of Hypertension–European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens 2003;21(6):1011–1153.
79. Arauz-Pacheco C, Parrott MA, Raskin P. Hypertension management in adults with diabetes. Diabetes Care 2004;27(Suppl 1):s65–s67.
80. American College of Cardiology. (2021). The world's first published expert consensus on ARNI treatment for hypertension. [online] Available from: https://www.acc.org/latest-in-cardiology/articles/2021/05/11/16/16/the-worlds-first-published-expert-consensus-on-arni-treatment-for-hypertension
81. Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. N Engl J Med 2017;377:644–657.
82. Jamerson K, Weber MA, Bakris GL, et al. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. N Engl J Med 2008;359(23):2417–2428.
83. King JB, Derington CG, Herrick JS, et al. Single-pill combination product availability of the antihypertensive regimens used for intensive systolic blood pressure treatment in the systolic blood pressure intervention trial. Hypertension 2023;80(8):1749–1758.
84. Asgedom SW, Atey TM, Desse TA. Antihypertensive medication adherence and associated factors among adult hypertensive patients at Jimma University Specialized Hospital, southwest Ethiopia. BMC Res Notes 2018;11:1–8.
85. Schmieder RE, Wassmann S, Predel HG, et al. Improved persistence to medication, decreased cardiovascular events and reduced all-cause mortality in hypertensive patients with use of single-pill combinations: results from the START-Study. Hypertension 2023;80(5):1127–1135.
86. Yusuf S, Bosch J, Dagenais G, et al. Cholesterol lowering in intermediate-risk persons without cardiovascular disease. N Engl J Med 2016;374(21):2021–2031.
87. The Heart Outcomes Prevention Evaluation Study Investigators. Vitamin E supplementation and cardiovascular events in high-risk patients. N Engl J Med 2000;342:154–160.
88. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomized placebo-controlled trial. Lancet 2002;360:7–22.
89. ASCEND Study Collaborative Group. Effects of aspirin for primary prevention in persons with diabetes mellitus. N Engl J Med 2018;379(16):1529–1539.
90. McNeil JJ, Nelson MR, Woods RL, et al. Effect of aspirin on all-cause mortality in the healthy elderly. N Engl J Med 2018;379(16):1519–1528.
91. Gaziano JM, Brotons C, Coppolecchia R, et al. Use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease (ARRIVE): a randomized, double-blind, placebo-controlled trial. Lancet 2018;392(10152):1036–1046.
92. Milman T, Joundi RA, Alotaibi NM, et al. Clinical inertia in the pharmacological management of hypertension: a systematic review and meta-analysis. Medicine (Baltimore) 2018;97(25):e11121.
93. Son H, Lee D, Lim LA, et al. Development of a pharmacokinetic interaction model for co-administration of simvastatin and amlodipine. Drug Metab Pharmacokinet 2014;29(2):120–128.
94. Cohen JS. Adverse drug effects, compliance, and initial doses of antihypertensive drugs recommended by the Joint National Committee vs the Physicians' Desk Reference. Arch Intern Med 2001;161(6):880–885.
95. Wright JM, Musini VM, Gill R. First-line drugs for hypertension. Cochrane Database Syst Rev 2018;4.
96. Musini VM, Tejani AM, Bassett K, et al. Pharmacotherapy for hypertension in adults 60 years or older. Cochrane Database Syst Rev 2019;6.
97. Musini VM, Gueyffier F, Puil L, et al. Pharmacotherapy for hypertension in adults aged 18 to 59 years. Cochrane Database Syst Rev 2017;8.
98. Preuss HG, Burris JF. Adverse metabolic effects of antihypertensive drugs: implications for treatment. Drug Saf 1996;14(6):355–364.
99. Rahimi K, Bidel Z, Nazarzadeh M, et al. Age-stratified and blood-pressure-stratified effects of blood-pressure-lowering pharmacotherapy for the prevention of cardiovascular disease and death: an individual participant-level data meta-analysis. Lancet 2021;398(10305):1053–1064.
100. Masoli JA, Sheppard JP, Rajkumar C. Hypertension management in older patients—are the guideline blood pressure targets appropriate? Age Ageing 2022;51(1):afab226.
101. Richter D, Guasti L, Walker D, et al. Frailty in cardiology: definition, assessment and clinical implications for general cardiology. Eur J Prev Cardiol 2022;29(1):216–227.
102. Opie LH. Drug interactions of antihypertensive agents: SA Hypertension Society Supplement. S Afr Fam Pract 2012;54(2):23–25.
103. Lauder L, Kandzari DE, Lüscher TF, et al. Renal denervation in the management of hypertension. EuroIntervention 2024;20(8):e467–e478.
104. Cluett JL, Blazek O, Brown AL, et al. Renal denervation for the treatment of hypertension: a scientific statement from the American Heart Association. Hypertension 2024;81(10):e135–e148.
105. Townsend RR, Mahfoud F, Kandzari DE, et al. Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED): a randomized, sham-controlled, proof-of-concept trial. Lancet 2017;390(10108):2160–2170.
106. Azizi M, Schmieder RE, Mahfoud F, et al. Endovascular ultrasound renal denervation to treat hypertension (RADIANCE-HTN SOLO): a multicentre, international, single-blind, randomized, sham-controlled trial. Lancet 2018;391(10137):2335–2345.
107. Azizi M, Sanghvi K, Saxena M, et al. Ultrasound renal denervation for hypertension resistant to a triple medication pill (RADIANCE-HTN TRIO): a randomised, multicentre, single-blind, sham-controlled trial. Lancet 2021;397(10293):2476–2486.
108. Mahfoud F, Böhm M, Schmieder R, et al. Effects of renal denervation on kidney function and long-term outcomes: 3-year follow-up from the Global SYMPLICITY Registry. Eur Heart J 2019;40(42):3474–3482.
109. Kandzari DE, Böhm M, Mahfoud F, et al. Effect of renal denervation on blood pressure in the presence of antihypertensive drugs: 6-month efficacy and safety results from the SPYRAL HTN-ON MED proof-of-concept randomised trial. Lancet 2018;391(10137):2346–2355.
110. Barbato E, Azizi M, Schmieder RE, et al. Renal denervation in the management of hypertension in adults. A clinical consensus statement of the ESC Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 2023;44(15):1313–1330.
111. Wallbach M, Born E, Kaempfer D, et al. Long-term effects of baroreflex activation therapy: 2-year follow-up data of the BAT Neo system. Clin Res Cardiol 2020;109:513–522.
112. Kapil V, Sobotka PA, Lobo MD, et al. Central arteriovenous anastomosis to treat resistant hypertension. Curr Opin Nephrol Hypertens 2018;27(1):8–15.
113. Janas A, Król M, Hochuł M, et al. Evaluation of transcatheter alcohol-mediated perivascular renal denervation to treat resistant hypertension. J Clin Med 2020;9(6):1881.
114. Calhoun DA, et al. Resistant hypertension: diagnosis, evaluation, and treatment. Hypertension 2008;51:1403–1419.
115. Vongpatanasin W. Resistant hypertension: a review of diagnosis and management. JAMA 2014;311(21):2216–2224.
116. International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension 2020;75(6):1334–1357.

117. Hegde S, Ahmed I, Aeddula NR. Secondary hypertension. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023. /
118. Taler SJ. Secondary causes of hypertension. Prim Care 2008;35(3):489–500.
119. Dopp JM, Reichmuth KJ, Morgan BJ. Obstructive sleep apnea and hypertension: mechanisms, evaluation, and management. Curr Hypertens Rep 2007;9(6):529–534.
120. Oscullo G, Torres G, Campos-Rodriguez F, et al. Resistant/refractory hypertension and sleep apnoea: current knowledge and future challenges. J Clin Med 2019;8(11):1872.
121. Streeten DHP, Anderson GH, Elias MF. Prevalence of secondary hypertension and unusual aspects of the treatment of hypertension in elderly individuals. Geriatr Nephrol Urol 1992;2:91–98.
122. Funder J. Primary aldosteronism: treatment of the disease, and new therapeutic approaches. Best Pract Res Clin Endocrinol Metab 2019;34(2):101368.
123. Aygun N. Pheochromocytoma and paraganglioma: from epidemiology to clinical findings. Sisli Etfal Hastan Tip Bul 2020;54(2):159–168.
124. Newell-Price J, Bertagna X, Grossman AB, et al. Cushing's syndrome. Lancet 2006;367(9522):1605–1617.
125. Rivas AM, Pena C, Kopel J, et al. Hypertension and hyperthyroidism: association and pathogenesis. Am J Med Sci 2020;361(1):3–7.
126. Simeoni M, Perna AF, Fuiano G. Secondary hyperparathyroidism and hypertension: an intriguing couple. J Clin Med 2020;9(3):629.
127. Somers VK, White DP, Amin R, et al. Sleep apnea and cardiovascular disease. Circulation 2008;118(10):1080–1111.
128. Foy MC, Vaishnav J, Sperati CJ. Drug-induced hypertension. Endocrinol Metab Clin North Am 2019;48(4):859–873.
129. Prisant LM, Mawulawde K, Kapoor D, et al. Coarctation of the aorta: a secondary cause of hypertension. J Clin Hypertens (Greenwich) 2004;6(6):347–352.
130. Braunthal S, Brateanu A. Hypertension in pregnancy: pathophysiology and treatment. SAGE Open Med 2019;7:2050312119843700.
131. Hall WD. Resistant hypertension, secondary hypertension, and hypertensive crises. Cardiol Clin 2002;20(2):281–289.
132. Nieman LK, Biller BMK, Findling JW, et al. Treatment of Cushing's syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2015;100(8):2807–2831.
133. Chugh KS, Jain S, Sakhuja V, et al. Renovascular hypertension due to Takayasu's arteritis among Indian patients. QJM 1992;85:833–843.
134. Cooper CJ, Murphy TP, Cutlip DE, et al. Stenting and medical therapy for atherosclerotic renal-artery stenosis. N Engl J Med 2014;370:13–22.
135. Leslie SW, Muppidi V, Gupta S. Hyperaldosteronism. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
136. Gupta PK, Marwaha B. Pheochromocytoma. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024.
137. Fleseriu M, Auchus R, Bancos I, et al. Consensus on diagnosis and management of Cushing's disease: a guideline update. Lancet Diabetes Endocrinol 2021;9(12):847–875.
138. Frohlich ED. Classic papers symposium, history of medicine series: surrogate indexes of target organ involvement in hypertension. Am J Med Sci 1996;312:225–228.
139. Zanchetti A, Sleight P, Birkenhaker WH. Evaluation of organ damage in hypertension. J Hypertens 1993;11:875–882.
140. Kannel WB. Left ventricular hypertrophy as a risk factor: the Framingham experience. J Hypertens 1991;9(Suppl 2):53–59.
141. Reddy KS. Cardiovascular diseases in India. World Health Stat Q 1993;46:101–107.
142. Eastern Stroke and Coronary Heart Disease Collaborative Research Group. Blood pressure, cholesterol and stroke in Eastern Asia. Lancet 1998;352:1801–1807.
143. MacMahon S, Peto R, Cutler J, et al. Blood pressure, stroke, and coronary heart disease. Part 1, prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. Lancet 1990;335:765–774.
144. Prospective Studies Collaboration. Cholesterol, diastolic blood pressure and stroke: 13,000 strokes in 45,000 people in 45 prospective cohorts. Lancet 1995;346:1647–1653.
145. Rosansky SJ, Hoover DR, King L, et al. The association of blood pressure levels and change in renal functions in hypertension and nonhypertensive subjects. Arch Intern Med 1990;150:2073–2074.
146. Kannel WB, Stampfer MJ, Castelli WP, et al. The prognostic significance of proteinuria: the Framingham study. Am Heart J 1984;108:1347–1352.
147. Yamada T, Ishihara M, Ichikawa K, et al. Proteinuria and renal function during antihypertensive treatment for essential hypertension. J Am Geriatr Soc 1980;28(3):114–117.
148. Lewis EJ, Hunsicker LG, Rodby RA, et al. A clinical trial of diabetic nephropathy. Am J Kidney Dis 2001;38(4 Suppl 1):S191–S194.
149. Wong TY, Mitchell P. Hypertensive retinopathy. N Engl J Med 2004;351:2310–2317.
150. Oakley CM. Aortic dissection. QJM 1991;79:357–380.
151. Ahmed I, Alley WD, Chauhan S, et al. Hypertensive crisis. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
152. Lavin P. Management of hypertension in patients with acute stroke. Arch Intern Med 1986;146:66–68.
153. Herling IM. Intravenous nitroglycerine: clinical pharmacology and therapeutic consideration. Am Heart J 1980;108:141–149.
154. O'Mailia J, Sander G, Giles T. Nifedipine associated myocardial ischemic or infarction in the treatment of hypertensive emergencies. Ann Intern Med 1987;107:185–186.
155. Sleight P. The HOPE study (Heart Outcomes Prevention Evaluation). J Renin Angiotensin Aldosterone Syst 2000;1(1):18–20.
156. Fitchett D. Results of the ONTARGET and TRANSCEND studies: an update and discussion. Vasc Health Risk Manag 2009;5(1):21–29.
157. Webb AJS, Werring DJ. New insights into cerebrovascular pathophysiology and hypertension. Stroke 2022;53(4):1054–1064.
158. Eisen HJ, Flack JM, Atluri P, et al. Management of hypertension in patients with ventricular assist devices: a scientific statement from the American Heart Association. Circ Heart Fail 2022;15(5):e000074.
159. Khaku AS, Tadi P. Cerebrovascular disease. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
160. Anderson CS, Heeley E, Huang Y, et al. Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. N Engl J Med 2013;368(25):2355–2365.
161. Qureshi AI, Palesch YY, Barsan WG, et al. Intensive blood-pressure lowering in patients with acute cerebral hemorrhage. N Engl J Med 2016;375(11):1033–1043.
162. Ma L, Hu X, Song L, et al. The third intensive care bundle with blood pressure reduction in acute cerebral haemorrhage trial (INTERACT3): an international, stepped wedge cluster randomised controlled trial. Lancet 2023;402:27–40.
163. Sinha AD, Agarwal R. Hypertension treatment for patients with advanced chronic kidney disease. Curr Cardiovasc Risk Rep 2014;8(10).
164. McGuire DK. Oral semaglutide and cardiovascular outcomes in high-risk type 2 diabetes. N Engl J Med 2025;392(20):2001–2012.
165. Georgianos PI, Agarwal R. Hypertension in chronic kidney disease—treatment standard 2023. Nephrol Dial Transplant 2023;38(12):2694–2703.
166. Kinsey D, Walther R, Sise ES, et al. Incidence of hyperuricemia in 400 hypertensive patients. Circulation 1961;24:972–976.
167. Zhu Y, Pandya BJ, Choi HK. Comorbidities of gout and hyperuricemia in the US general population: NHANES 2007-2008. Am J Med 2012;125:679–687.
168. Borghi C, Agnoletti D, Cicero AFG, et al. Uric acid and hypertension: a review of evidence and future perspectives for the management of cardiovascular risk. Hypertension 2022;79(9).
169. Høieggen A, Alderman MH, Kjeldsen SE, et al. The impact of serum uric acid on cardiovascular outcomes in the LIFE study. Kidney Int 2004;65:1041–1049.
170. Razo C, Welgan CA, Johnson CO, et al. Effects of elevated systolic blood pressure on ischemic heart disease: a burden of proof study. Nat Med 2022;28(10):2056–2065.
171. Hosseini N, Talaei M, Marshall T, et al. Risk of cardiovascular disease in treated and untreated individuals with hypertension. J Hypertens 2018;36(Suppl 1):e3.
172. Vidal-Petiot E, Ford I, Greenlaw N, et al. Cardiovascular event rates and mortality according to achieved systolic and diastolic blood pressure in patients with stable coronary artery disease: an international cohort study. Lancet 2016;388:2142–2152.
173. Sorbets E, Greenlaw N, Ferrari R, et al. Rationale, design, and baseline characteristics of the CLARIFY registry of outpatients with stable coronary artery disease. Clin Cardiol 2017;40:797–806.
174. Yusuf S, Peto R, Lewis J, et al. B blockade during and after myocardial infarction: an overview of the randomized trials. Prog Cardiovasc Dis 1985;27:335–371.
175. Deanfield JE, Detry J-MRG, Lichtlen PR, et al. Amlodipine reduces transient myocardial ischemia in patients with coronary artery disease: double-blind circadian anti-ischemia program in Europe (CAPE trial). J Am Coll Cardiol 1994;24:1460–1467.
176. Pitt B, Byington RP, Furberg CD, et al. Effect of amlodipine on the progression of atherosclerosis and the occurrence of clinical events. Circulation 2000;102:1503–1510.
177. Ryan TJ, Anderson JL, Antman EM, et al. ACC/AHA guidelines for the management of patients with acute myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). J Am Coll Cardiol 1996;28:1328–1428.
178. Pfeffer MA, Braunwald E, Moye LA, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction: results of the survival and ventricular enlargement trials. N Engl J Med 1992;327:669–677.
179. Lonn EM, Yusuf S, Jha P, et al. Emerging role of angiotensin-converting enzyme inhibitors in cardiac and vascular protection. Circulation 1994;90:2056–2069.
180. Di Palo KE, Barone NJ. Hypertension and heart failure: prevention, targets, and treatment. Cardiol Clin 2022;40(2):237–244.
181. Anker SD, Usman MS, Anker MS, et al. Patient phenotype profiling in heart failure with preserved ejection fraction to guide therapeutic decision making. Eur J Heart Fail 2023.
182. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2022;145(18):e895–e1032.
183. Am J, Ps J, Is A, et al. Sacubitril-valsartan as a treatment for apparent resistant hypertension in patients with heart failure and preserved ejection fraction. Eur Heart J 2021;42(36):3741–3752.
184. Gawałko M, Linz D. Atrial fibrillation detection and management in hypertension. Hypertension 2023;80(3):523–533.
185. Middeldorp ME, Ariyaratnam JP, Kamsani SH, et al. Hypertension and atrial fibrillation. J Hypertens 2022;40(12):2337–2352.
186. Aune D, Mahamat-Saleh Y, Kobeissi E, et al. Blood pressure, hypertension and the risk of atrial

fibrillation: a systematic review and meta-analysis of cohort studies. Eur J Epidemiol 2023;38(2):145–178.
187. Pittaras A, Grassos C, Faselis C, et al. Atrial fibrillation and mortality risk in hypertensive patients according to cardiorespiratory fitness. J Hypertens 2023;41(Suppl 3):e91.
188. Global Initiative for Chronic Obstructive Lung Disease (GOLD) Report. 2024.
189. Taher S, Schutte AE, Hurst JR, et al. Interventions for the management of concomitant COPD and hypertension: a systematic review. J Multimorb Comorb 2025;15:26335565251341389.
190. Uddin MJ, Alam N, Sarma H, et al. Consequences of hypertension and chronic obstructive pulmonary disease, healthcare-seeking behaviors of patients, and responses of the health system: a population-based cross-sectional study in Bangladesh. BMC Public Health 2014;14(1):547.
191. Coley K, John C, Ghouse J, et al. Genomics of chronic dry cough unravels neurological pathways. Eur Respir J 2025;66(3):2402341.
192. Verdecchia P, Cavallini C, Coiro S, et al. Certainties fading away: β-blockers do not worsen chronic obstructive pulmonary disease. Eur Heart J Suppl 2021;23(Suppl E):E172–E176.
193. Albouaini K, Andron M, Alahmar A, et al. Beta-blockers use in patients with chronic obstructive pulmonary disease and concomitant cardiovascular conditions. Int J Chron Obstruct Pulmon Dis 2007;2(4):535–540.
194. Hill NS. Fluid and electrolyte considerations in diuretic therapy for hypertensive patients with chronic obstructive pulmonary disease. Arch Intern Med 1986;146(1):129–133.
195. Morgan AD, Zakeri R, Quint JK. Defining the relationship between COPD and CVD: what are the implications for clinical practice? Ther Adv Respir Dis 2018;12:1753465817750524.
196. Jones KE, Hayden SL, Meyer HR, et al. The evolving role of calcium channel blockers in hypertension management: pharmacological and clinical considerations. Curr Issues Mol Biol 2024;46(7):6315–6327.
197. Dalal JJ, Padmanabhan TNC, Jain P, et al. Lipitension: interplay between dyslipidemia and hypertension. Indian J Endocrinol Metab 2012;16(2):240–245.
198. UNFPA India. (2023). India ageing, elderly to make up 20% of population by 2050: UNFPA report. [online] Available from: https://india.unfpa.org/en/news/india-ageing-elderly-make-20-population-2050-unfpa-report [Last accessed April 2026]
199. Ringer M, Hashmi MF, Lappin SL. Orthostatic hypotension. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
200. Freeman R. Current pharmacologic treatment for orthostatic hypotension. Clin Auton Res 2008;18(S1):14–18.
201. Gupta V, Lipsitz LA. Orthostatic hypotension in the elderly: diagnosis and treatment. Am J Med 2007;120(10):841–847.
202. Wieling W, Van Dijk N, Thijs RD, et al. Physical countermeasures to increase orthostatic tolerance. J Intern Med 2014;277(1):69–82.
203. Jordan J, Biaggioni I. Diagnosis and treatment of supine hypertension in autonomic failure patients with orthostatic hypotension. J Clin Hypertens (Greenwich) 2002;4(2):139–145.
204. Chaudhary M, Sharma P. Abdominal obesity in India: analysis of the National Family Health Survey-5(2019-2021) data. Lancet Reg Health Southeast Asia 2023;14:100208.
205. Joseph JJ, Deedwania P, Acharya T, et al. Comprehensive management of cardiovascular risk factors for adults with type 2 diabetes: a scientific statement from the American Heart Association. Circulation 2022;145(9):e722–e759.
206. Kennedy C, Hayes P, Salama S, et al. The effect of semaglutide on blood pressure in patients without diabetes: a systematic review and meta-analysis. J Clin Med 2023;12(3):772.
207. de Lemos JA, Linetzky B, le Roux CW, et al. Tirzepatide reduces 24-hour ambulatory blood pressure in adults with body mass index ≥27 kg/m^2: SURMOUNT-1 ambulatory blood pressure monitoring substudy. Hypertension 2024;81(4):e41–e43.
208. Schiavon CA, Bersch-Ferreira AC, Santucci EV, et al. Effects of bariatric surgery in obese patients with hypertension: the GATEWAY randomized trial (Gastric Bypass to Treat Obese Patients With Steady Hypertension). Circulation 2018;137(11):1132–1142.
209. Bhalwar R. Metabolic syndrome: the Indian public health perspective. MJAFI 2020;76(1):8–16.
210. Yeghiazarians Y, Jneid H, Tietjens JR, et al. Obstructive sleep apnea and cardiovascular disease: a scientific statement from the American Heart Association. Circulation 2021;144.
211. Suri TM, Ghosh T, Mittal S, et al. Systematic review and meta-analysis of the prevalence of obstructive sleep apnea in Indian adults. Sleep Med Rev 2023;71:101829.
212. Carey RM, Calhoun DA, Bakris GL, et al. Resistant hypertension: detection, evaluation, and management: a scientific statement from the American Heart Association. Hypertension 2018;72(5):e53–e90.
213. Małyszko J, Małyszko M, Kozlowski L, et al. Hypertension in malignancy-an underappreciated problem. Oncotarget 2018;9(29):20855–20871.
214. Cohen JB, Brown NJ, Brown SA, et al. Cancer therapy-related hypertension: a scientific statement from the American Heart Association. Hypertension 2023;80(3):e46–e57.
215. Lewis KS. Pharmacological review of postoperative hypertension. J Pharm Pract 2002;15(2):135–146.
216. Haas CE, LeBlanc JM. Acute postoperative hypertension: a review of therapeutic options. Am J Health Syst Pharm 2004;61(16):1661–1673.
217. Resistant hypertension. Cleveland Clinic; 2026.
218. Kitt J, Fox R, Tucker KL. Digital health: new approaches in hypertension management. J Cardiol Cardiovasc Sci 2020;4(1).
219. Hare AJ, Chokshi N, Adusumalli S. Novel digital technologies for blood pressure monitoring and hypertension management. Curr Cardiovasc Risk Rep 2021;15(8):11.
220. Karam S, Drawz PE. Telemonitoring for hypertension management: the time is now. Kidney360 2022;3(11):1961–1964.
221. Visco V, Izzo C, Mancusi C, et al. Artificial intelligence in hypertension management: an ace up your sleeve. J Cardiovasc Dev Dis 2023;10(2):74.
222. Saputra PB, Yolanda S, Purwati DD. The roles of social media in hypertension management programs. Cermin Dunia Kedokteran 2022;49(8):469–473.