REVIEW/EXPERT OPINION REVIEW

Management of Hypertension and Associated Comorbidities: An Expert Consensus Statement from India

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Abstract

Hypertension is a leading global health concern that significantly contributes to cardiovascular (CV) and renal diseases. In India, its prevalence is rising, often coexisting with comorbidities such as type 2 diabetes mellitus (T2DM), chronic kidney disease (CKD), coronary artery disease (CAD), and metabolic syndrome (MetS).

Effective hypertension management in these populations is challenging due to variations in blood pressure (BP) targets, the need for combination therapy, and the complexity of treating associated conditions such as albuminuria, nephropathy, CKD, CAD, and acute coronary syndromes (ACS). Despite advancements in treatment options, inconsistencies in clinical practice highlight the need for standardized, evidence-based recommendations.

This expert consensus aims to address these gaps by guiding BP targets, optimal antihypertensive strategies, and individualized treatment approaches for high-risk patients. Key considerations include the role of renin–angiotensin–aldosterone system blockers, calcium channel blockers (CCBs), beta-blockers (BBs), sodium–glucose cotransporter-2 inhibitors, and combination therapies in improving CV and renal outcomes.

By establishing clear, consensus-driven recommendations, this statement seeks to enhance hypertension management, promote early intervention, and improve patient outcomes in India.

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Introduction

Hypertension is a significant global health concern, contributing to 10–12% of all-cause mortality. In India, hypertension affects 32.6% of women and 38.7% of men over the age of 20, with prevalence varying across different states.[1] Genetic factors and poor lifestyle choices are known risk factors.[2] Therefore, managing these risk factors is vital in hypertension treatment.[1,3] Moreover, individuals with hypertension are at increased risk of developing comorbidities than those with normal blood pressure (BP).[4,5]

Hypertension and type 2 diabetes mellitus (T2DM) often coexist and are key drivers of mortality and disability.[2,6] Hypertension is considerably more common among individuals with T2DM (Fig. 1). In India, individuals with diabetes are 1.5–2 times more likely to have hypertension, reflecting a rising trend in their coexistence.[7] This relationship extends beyond BP elevation, as hypertension exacerbates diabetic complications such as nephropathy, retinopathy, and neuropathy, while T2DM accelerates vascular dysfunction, further aggravating hypertension.[2,5,8]

Moreover, hypertension seldom occurs alone and is frequently accompanied by other cardiovascular (CV) risk factors. These include insulin resistance, dyslipidemia, microalbuminuria, central obesity, hypercoagulation, increased inflammation, and left ventricular hypertrophy (LVH), which collectively increase the overall CV risk and predispose individuals to coronary artery disease (CAD) and heart failure (HF).[2,9–11] Hypertension contributes approximately 25% to CAD risk, while its effective management can reduce this risk by 17%.[11]

Beyond its CV implications, hypertension is closely linked to kidney function, as prolonged high BP can lead to chronic kidney disease (CKD), while impaired renal function exacerbates BP dysregulation, creating a vicious cycle that necessitates continuous monitoring and management.[12] Despite its widespread impact, hypertension often remains undiagnosed due to its modest symptoms, increasing the risk of severe comorbidities if left uncontrolled.[1,13]

Given its consequences across multiple organ systems, comprehensive care strategies targeting hypertension and associated conditions are essential to mitigating overall disease burden and death rates.[11,14] In this context, patients with comorbidities often require more complex treatment regimens.[3,15] However, recent studies in India have highlighted that several factors, including comorbidities and polypharmacy, significantly undermine treatment adherence and discontinuation.[15,16] Low treatment adherence is also a key contributor to poor BP control, which, over time, leads to uncontrolled hypertension.[17] Recent Indian data also indicate that comorbidities are a significant predictor of uncontrolled hypertension, with diabetes (40.8% of cases) and CKD (18.1% of cases) showing strong associations when compared with controlled hypertension.[17,18] Additional factors, such as therapeutic inertia and limited access to optimized antihypertensive regimens in the Indian scenario, further exacerbate the burden of uncontrolled hypertension.[17] Therefore, understanding the impact of comorbidities on hypertension, identifying treatment targets, and optimizing treatment approaches can help with therapy recommendations for these patients.[11,19]

The primary objective of this expert consensus meeting was to discuss and establish evidence-based treatment goals and strategies for managing hypertension in patients with various associated comorbidities,

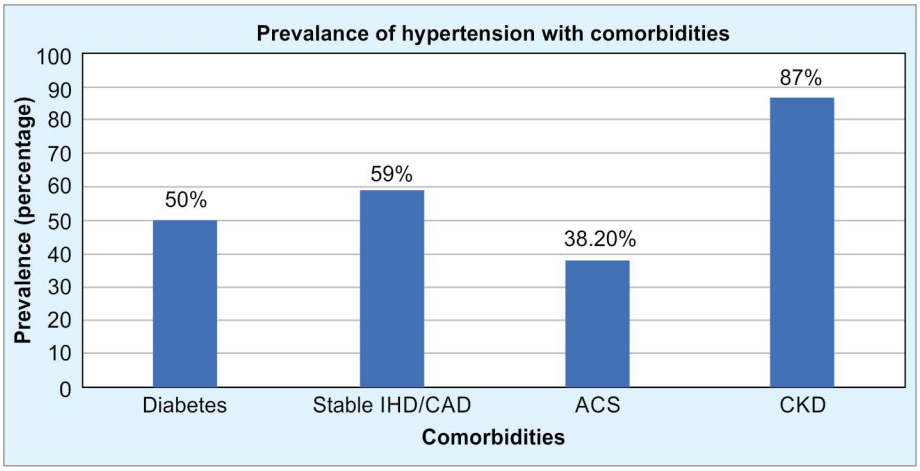

Fig. 1: Prevalence of hypertension with other conditions in Indians[7,20,21]

including T2DM, CKD, metabolic syndrome (MetS), and CAD.

Methodology

The national consensus meetings were organized from November 2024 to February 2025 to discuss the current evidence-based approach for managing nocturnal hypertension. A total of 23 meetings were organized, and a total of 700 experts from cardiology, nephrology, endocrinology, and consulting physicians attended the meeting. One senior cardiologist presented the most comprehensive and updated evidence on hypertension and its association with different coexisting conditions, including T2DM, MetS, CKD, CAD, and acute coronary syndrome (ACS). The experts discussed the BP targets or goals in these comorbidities based on the evidence and guideline recommendations. The panel also examined the pharmacological management of hypertension in these associated comorbidities.[20,21]

About 10 statements were discussed and deliberated upon based on the current evidence. After this discussion, experts put to a vote using a 5-point Likert scale, where (A) agree completely, (B) agree with minor reservation, (C) agree with major reservation, (D) disagree with minor reservation, and (E) disagree with major reservation. Consensus on a statement was considered to be achieved if the sum of responses for "(A) agree completely" and "(B) agree with minor reservations" was 75% or higher.

Pathophysiology of Hypertension and Comorbidities

Hypertension shares common pathophysiological mechanisms with several chronic diseases, particularly T2DM, CKD, and CAD. These conditions often cooccur due to overlapping risk factors and interconnected biological pathways.

Type 2 Diabetes Mellitus

Metabolic factors like obesity, visceral adiposity, and insulin resistance contribute to both hypertension and T2DM.[6,22] These factors promote the overactivation of renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system (SNS), as well as oxidative stress, chronic inflammation, and renal sodium retention.[22,23] Together, these processes lead to elevated BP and impaired glucose metabolism. Furthermore, hypertension causes endothelial dysfunction and microvascular damage, which worsens insulin resistance and may lead to diabetes.[11,22] On the contrary, diabetes accelerates arterial stiffness and kidney damage, further raising BP (Fig. 2).[22]

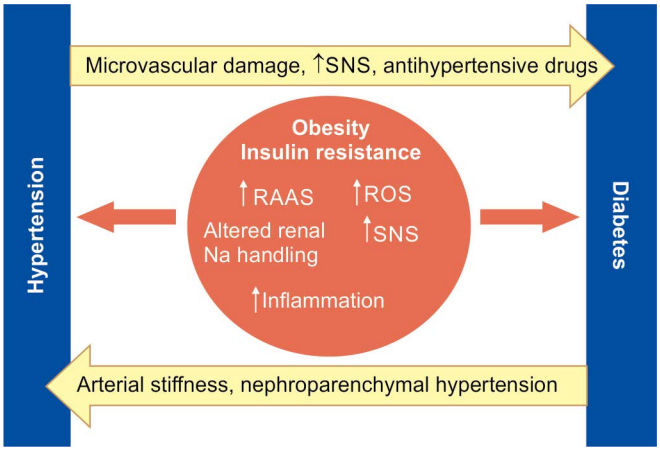

Fig. 2: Association of hypertension and diabetes[22]

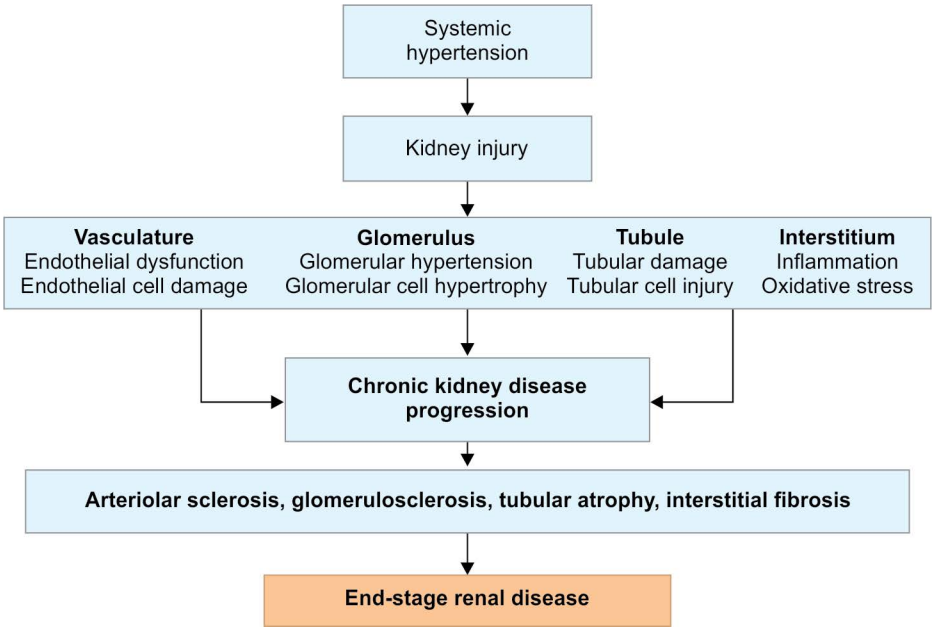

Fig. 3: Pathophysiology of hypertension in CKD[24]

Chronic Kidney Disease

The kidneys help regulate long-term BP and fluid balance through autoregulation, which maintains a stable glomerular filtration rate (GFR) and blood flow. In chronic hypertension, this mechanism breaks down, leading to increased intraglomerular pressure and damage to the glomeruli. This damage worsens kidney function, further raising BP due to activation of the RAAS, SNS, and sodium handling issues.[24] Over time, structural changes such as arteriolar sclerosis and fibrosis develop, progressing to end-stage renal disease (ESRD).[25] In CKD, hypertension both results from and contributes to kidney damage, creating a vicious cycle that accelerates disease progression (Fig. 3).[24]

Coronary Artery Disease

Hypertension is a significant risk factor for CAD and often represents its earliest complication.[26] The development of CAD in patients with hypertension involves genetic and environmental factors that influence neurohormonal pathways, hemodynamics, vascular structure, and inflammation.[26,27]

- Chronic high BP causes mechanical and hemodynamic stress on arteries, leading to stiffness, poor coronary perfusion, and atherosclerosis.[28]
- Endothelial dysfunction in hypertension impairs vasodilation and antithrombotic, antioxidant, and anti-inflammatory functions, promoting myocardial ischemia.[28]
- Oscillatory blood flow and reactive oxygen species (ROS) production trigger proinflammatory responses, vascular

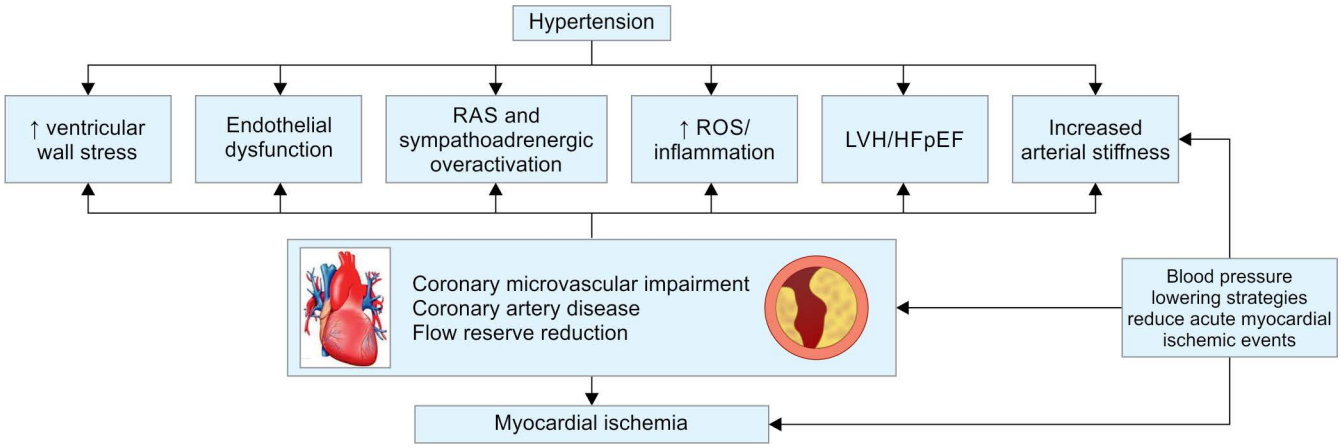

Fig. 4: Mechanisms linking hypertension and CAD[28]

smooth muscle cell proliferation, and vascular remodeling.[28]

- These processes collectively result in vascular and organ damage driven by sustained hypertension (Fig. 4).[28]

Thus, hypertension plays both a causal and consequential role in T2DM, CKD, and CAD, driven by shared mechanisms of vascular injury, neurohormonal imbalance, and metabolic dysregulation.

Albuminuria in Hypertension and Associated Comorbidities

Albuminuria is common in individuals with hypertension and diabetes, two well-known contributors to cardiovascular disease (CVD).[29] While it is frequently associated with diabetic kidney disease, albuminuria also has a strong, independent link to hypertension.[29,30] It is relatively common among Indian patients with hypertension, with prevalence ranging from 23 to 47%, being higher among those with T2DM (31–48%), highlighting the added renal risk associated with comorbid T2DM.[31–34] Albuminuria becomes more common with age and as hypertension persists and worsens.[30,35] Its severity is linked to BP levels and improves with BP management.[30]

The primary causes of albuminuria in hypertension are likely changes in hemodynamics that elevate intraglomerular pressure, along with generalized angiopathy resulting from endothelial dysfunction, which leads to both renal and systemic transvascular albumin leakage.[35] Individuals with hypertension and microalbuminuria are at greater risk for target organ damage. For example, patients with albuminuria commonly exhibit increased left ventricular mass, as well as increased risk of hypertensive retinopathy and myocardial infarction (MI).[29] Literature also indicates that each 0.4 mg/mmol increase in the albumin-to-creatinine ratio (ACR) leads to a 6% higher risk of experiencing cardiovascular events (CVEs).[35]

Albuminuria is a significant predictor of renal disease progression. A urine albumin-to-creatinine ratio (UACR) >30 mg/gm sustained for over 3 months signals the development of CKD, even when estimated glomerular filtration rate (eGFR) remains normal. A Swedish cohort study found that a fourfold increase in UACR significantly raises the risk of ESRD, while a fourfold decrease lowers the risk. These associations were consistent regardless of the presence of T2DM, hypertension, or changes in eGFR. Evidence from other studies highlights that both eGFR decline and albuminuria variation are key predictors of future CKD in T2DM.[36]

There are multiple therapeutic agents available that can reduce albuminuria, lower CV risk, and improve renal outcomes. However, screening for albuminuria remains limited.[30] Therefore, considering the association of albuminuria with an increased risk of major CVEs and ESRD, performing routine screening for albuminuria is recommended.[37]

Blood Pressure Targets in Hypertension Associated with Comorbidities

Hypertension and Type 2 Diabetes Mellitus/Metabolic Syndrome

Lowering BP to <130/80 mm Hg is generally beneficial for diabetic patients, particularly in reducing stroke risk, as supported by studies like HOT and UKPDS (Table 1).[5,14,23,38,39] These trials demonstrated significant CV benefits. However, the achieved BP often remained higher than the target.[14] On the contrary, the ACCORD-BP study found that intensive BP therapy [systolic blood pressure (SBP) <120 mm Hg] reduced the risk of stroke but was associated with an increased occurrence of serious adverse events such as syncope and hyperkalemia (Table 1).[14,23,40] The ABCD trial also found that intensive BP control improved stroke and renal outcomes, particularly in slowing albuminuria progression (Table 1).[23,41] In elderly individuals (over 80 years), a BP target of <140–150/90 mm Hg is considered more appropriate, given the increased risk of adverse effects associated with lower BP levels (Table 2).[14] Achieving these targets can be challenging due to the increased risk of side effects, particularly in older adults or individuals with kidney problems, as aggressive BP control may lead to complications. Additionally, the complexity of treatment regimens can impact patient adherence, further complicating BP management.[42,43]

There are no distinct BP targets in current guidelines for patients with both hypertension and MetS; however, general hypertension treatment guidelines can be followed.[44]

Hypertension and Chronic Kidney Disease

Lowering BP, especially in patients with proteinuria, slows eGFR decline, as seen in studies like MDRD, AASK, and REIN-2 (Table 1).[25] Guidelines released after these studies reflected their findings, recommending lower BP targets only for patients with significant proteinuria. However, these studies did not consider the possible benefits of intensive BP control on CV outcomes.[25] In the context of CKD, guideline BP targets are more variable and range from <140/90 to <120 mm Hg, depending on the individual's tolerance (Table 2).

Hypertension and Coronary Artery Disease/Acute Coronary Syndrome

Several randomized studies have explored the effects of intensive compared to standard BP management in individuals at risk for CVD. Trials like ACCORD and SPRINT showed that intensive BP control reduced CV risk but increased adverse events (Table 1).[44,45] According to a secondary analysis of the INVEST trial, maintaining SBP below 140 mm Hg

Table 1: Clinical studies on BP targets in different comorbidities

Study	*Population, age, targets, follow-up*	*Findings*
BP target trials in T2DM		
ACCORDION (long-term follow-up of ACCORD), 2016[14]	<120 mm Hg (intensive)	Long-term follow-up showed a 9% nonsignificant reduction in CV events with continued intensive BP control
ACCORD-BP, 2010[40]	• 4733 participants with T2DM • Intensive therapy (SBP <120 mm Hg) • Standard therapy (SBP <140 mm Hg)	Annual rate of outcomes in intensive vs standard: • Primary outcome: 1.87 vs 2.09% (HR for intensive therapy: 0.88; 95% CI: 0.73–1.06; $p = 0.20$) • Death from any cause were 1.28 vs 1.19% (HR: 1.07; 95% CI: 0.85–1.35; $p = 0.55$) • Stroke: 0.32 vs 0.53% in the standard-therapy group (HR: 0.59; 95% CI: 0.39–0.89; $p = 0.01$) • Serious adverse events due to antihypertensive treatment: 3.3 vs 1.3% ($p < 0.001$)
ABCD, 2007[41]	• 950 patients with T2DM • 5 years of follow-up	1. In the hypertensive ABCD study: intensive BP control significantly reduced mortality compared to standard control 2. In the normotensive ABCD study: • Intensive BP control slowed the progression of nephropathy and retinopathy • Fewer strokes occurred in the intensive control group 3. In both hypertensive and normotensive studies: • Mean renal function remained stable over 5 years with either intensive or standard BP control in patients with normoalbuminuria or microalbuminuria at baseline • Patients with overt diabetic nephropathy at baseline showed a decrease in creatinine clearance by 5 mL/minute/year, regardless of BP control intensity
HOT, 1998[38]	• 18,790 patients • Age: 50–80 years (mean age: 61.5 years) • 26 countries • DBP: 100–115 mm Hg (mean: 105 mm Hg) • Subset of diabetes patients ($N = 1,501$) • Target BP: 80 and 90 mm Hg	1. For major CVEs, the lowest point of risk was at a mean achieved DBP of 82.6 mm Hg and at a mean SBP of 138.5 mm Hg 2. Diabetes specific: • 50% reduction in major CVEs in the group with a target of 80 mm Hg compared to the target group of 90 mm Hg. • 30% risk reduction in the rate of strokes in the 80 mm Hg target group compared to the 90 mm Hg group 3. Significantly lower CV mortality in the 80 mm Hg target group (3.7 vs 11.1 events/100 patient-years)
UKPDS 38, 1998[39]	• 1,148 patients with T2DM and hypertension • Mean age: 56 years • Mean BP at entry: 160/94 mm Hg • Median follow-up of 8.4 years • Tight control of BP ($N = 758$) • Less tight control ($N = 390$)	1. Significantly lower mean BP in the tight control group (144/82 mm Hg) compared to the less tight control group (154/87 mm Hg) ($p < 0.0001$) 2. Tight control resulted in: • 24% reduction in diabetes-related endpoints ($p = 0.0046$) • 32% reduction in deaths related to diabetes ($p = 0.019$) • 44% reduction in strokes ($p = 0.013$) • 37% reduction in microvascular endpoints ($p = 0.0092$) 3. After 9 years, tight control led to: • 34% reduction in retinopathy deterioration by two steps ($p = 0.0004$) • 47% reduction in deterioration of visual acuity by three lines on the ETDRS chart ($p = 0.004$)
BP target trials in hypertension with CKD		
MDRD and AASK extended follow-up (2015 and 2017, respectively)[25]	• Patients with CKD from the MDRD and AASK studies • Intensive BP control vs standard BP control	Long-term follow-up suggests survival benefits from intensive BP lowering but no change in CKD progression rate

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BP target trials in hypertension with CKD		
REIN-2 study 2005[25]	• Proteinuria >1 gm/day, eGFR <70 mL/minute/1.73 m^2, nondiabetic, on ACEi • DBP <90 vs BP <130/80 mm Hg with the addition of CCB • Follow-up: 335 patients, median 1.6 years	Adding CCB reduced BP but did not improve renoprotection compared to standard BP control with an ACE inhibitor
AASK study 2002[25]	• Participants: eGFR 20–65 mL/minute/1.73 m^2, nondiabetic • MAP: 102–107 vs 97 mm Hg • Follow-up: 1,094 patients, minimum 3 years	Only patients with baseline proteinuria >1 gm/day demonstrated slowing of CKD with intensive BP control
MDRD study 1994[25]	• US population with CKD (eGFR 13–55 mL/minute/1.73 m^2) • Standard MAP 107 mm Hg vs intensive MAP 92 mm Hg • Follow-up: 840 patients, mean 2.2 years	• Intensive BP control slowed eGFR decline in patients with proteinuria >1 gm/day, but not in those without proteinuria • Found no significant difference in eGFR decline, ESKD progression, or mortality over 3 years
BP target trials in hypertension with CAD		
VALUE trial, 2016[45]	• 15,245 hypertensive patients (~50% with CAD) • Valsartan vs amlodipine • DBP ≥90 vs <90 mm Hg • DBP ≥70 vs <70 mm Hg	• No significant differences in primary CV outcomes* between valsartan and amlodipine • Patients with DBP ≥90 mm Hg had more CV events than those with DBP <90 mm Hg • No difference in primary outcome between DBP <70 and ≥70 mm Hg • Lower DBP thresholds for MI and stroke were identified (76 and 60 mm Hg, respectively), suggesting different organ vulnerabilities at varying DBP levels
Bengaluru et al./ secondary analysis from the INVEST, 2014[45]	• Hypertensive patients aged >60 years with known CAD • A target SBP of <140 vs 140 to <150 or ≥150 mm Hg	1. SBP <140 vs 140 to <150 or ≥150 mm Hg • Lowest rate of primary outcome[#] (9.36 vs 12.71 vs 21.32%; $p < 0.0001$) • Lower CV mortality (7.92 vs 10.07 vs 16.81%; $p < 0.0001$), MI (1.07 vs 1.03 vs 2.91%; $p < 0.0001$), and all-cause mortality (3.26 vs 4.58 vs 7.80%; $p < 0.0001$), total stroke (1.19 vs 2.63 vs 3.85%; $p < 0.0001$), and nonfatal stroke (0.86 vs 1.89 vs 2.86%; $p < 0.0001$) 2. SBP 140–150 mm Hg was linked to increased CV mortality (HR 1.34, 95% CI: 1.01–1.77, $p = 0.04$) and total stroke risk (HR 1.89, 95% CI: 1.26–2.82, $p = 0.002$) and nonfatal stroke (HR: 1.70, 95% CI: 1.06–2.72, $p = 0.03$)

AASK, African American Study of Kidney Disease and Hypertension; ABCD, appropriate blood pressure control in diabetes; ACCORD-BP, action to control cardiovascular risk in diabetes—blood pressure; ACCORDION, follow-up study of the ACCORD trial; ESKD, end-stage kidney disease; ETDRS, early treatment diabetic retinopathy study; HOT, hypertension optimal treatment; MAP, mean arterial pressure; MDRD, modification of diet in renal disease; UKPDS, United Kingdom Prospective Diabetes Study; *Primary CV outcomes: time to first cardiac event, that is, a composite of fatal or nonfatal MI, sudden cardiac death, death from revascularization procedures, heart failure requiring hospitalization, and emergency procedures to prevent MI; [#]First occurrence of all-cause death, nonfatal MI, or nonfatal stroke

is linked to reduced risks of CV mortality and MI (Table 1).[45]

Most trials did not resolve concerns about the J-curve effect. Findings from the VALUE trial do not align with the J-curve hypothesis (Table 1).[45] Few clinical studies have assessed the implications of diastolic blood pressure (DBP) reduction in hypertensive individuals with CAD. Findings of the ARIC trial suggest advised caution when lowering SBP below 140 mm Hg to avoid DBP dropping below 60–70 mm Hg (Table 1).[45]

In older adults with CAD, maintaining an SBP between 120 and 140 mm Hg is linked to improved clinical outcomes compared to levels above 140 mm Hg, without increasing mortality risk from lower diastolic BP.[45–50]

Specific BP targets for ACS patients remain undefined,51 but a target of 140/90 mm Hg is recommended for hemodynamically stable individuals, with 130/80 mm Hg advised at hospital discharge. BP should be lowered gradually, ensuring DBP does not drop below 60 mm Hg.[52]

Pharmacological Management of Hypertension Associated with Comorbidities

Angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), and diuretics are all viable choices for initial BP management in patients with hypertension and comorbidities. Antihypertensive agents should be selected considering potential cardiometabolic effects, particularly in patients with T2DM, MetS, CAD, and CKD.[5,6]

Renin–Angiotensin–Aldosterone System Blockers

Renin–angiotensin–aldosterone system blockers are strongly recommended as first-line treatment for patients with hypertension, T2DM, CKD, and CAD (Table 2).[44,53–55]

Renin-angiotensin-aldosterone system inhibitors are particularly valuable in patients with CKD as they slow the progression of nephropathy by lowering intraglomerular pressure and reducing proteinuria, independent of their BP-lowering effect. This makes them the preferred choice for

Table 2: Guideline comparison for hypertension targets

Guideline	*BP target*	*Management of hypertension*
T2DM		
ESC 2024[46]	• Target SBP to 130 and <130 mm Hg if tolerated, but not <120 mm Hg • Target SBP range of 130–139 mm Hg in older people (aged ≥65 years)	Not mentioned
ADA 2024[47]	<130/80 mm Hg	• ACE inhibitor or ARB as the first-line treatment for hypertensive patients with diabetes and urinary ACR 300 mg/creatinine or 30–299 mg/gm creatinine • If one class is not tolerated, the other should be substituted
InSH 2023[1]	<130/80 mm Hg	SGLT2is recommended to reduce the occurrence of cardiac and kidney-related events
ESH 2023[48]	<130/80 mm Hg	• SGLT2is are recommended to reduce cardiac and kidney events in T2DM • Finerenone can be used in patients with diabetic CKD and moderate to severe albuminuria
RSSDI 2022[7]	• <130/80 mm Hg • <140/90 mmHg for elderly	• ARBs either alone or in combination with CCBs • ARBs must be preferred over ACEIs • Telmisartan or azilsartan selected as the first-line agent • CCBs must be preferred over BBs and thiazides in combination therapy with ARBs
ACC/AHA 2017[49]	<130/80 mm Hg	• All first-line classes of antihypertensive agents (i.e., diuretics, ACEIs, ARBs, and CCBs) are useful and effective • ACEIs or ARBs may be considered in the presence of albuminuria
CKD		
ESC 2024[46]	SBP range of 130–139 mm Hg in patients with diabetic or nondiabetic CKD	RAS blockers for hypertensive patients with microalbuminuria or proteinuria SGLT2is in hypertensive patients with CKD and eGFR >20 mL/minute/1.73 m^2
KDIGO 2024[50]	SBP of <120 mm Hg, when tolerated, using standardized office BP measurements (in high BP and CKD patients)	RAAS inhibitors (ACEIs or ARB) for the following patients: CKD and severely increased albuminuria without diabetes CKD and moderately increased albuminuria without diabetes CKD and moderately-to-severely increased albuminuria with diabetes
InSH 2023[1]	• <130/80 mm Hg • <140/80 in elderly patients	• ACEI or ARB, with doses adjusted to the maximum tolerable levels, advised in CKD patients who exhibit moderate or severe albuminuria • SGLT2i recommended for diabetic or nondiabetic nephropathies associated with CKD, when eGFR is at least 20 or 25 mL/minute/1.73 m^2 • Finerenone is suggested for CKD patients with albuminuria related to T2DM when the eGFR is at least 25 mL/minute/1.73 m^2 and serum potassium levels are below 5.0 mmol/L
ESH 2023[48]	• Lower office BP to <140/90 mm Hg in all CKD patients • Further reduction to <130/80 mm Hg is advised, if tolerated • BP target <120/70 mm Hg is not recommended in patients with CKD	• ACEI or an ARB for patients with CKD and moderate or severe albuminuria (titrated to the maximum tolerated doses) • SGLT2is for patients with diabetic and nondiabetic nephropathies CKD, if eGFR is at least 20 mL/minute/1.73 m^2 • Finerenone is recommended in patients with CKD and albuminuria associated with T2DM if eGFR is at least 25 mL/min/1.73 m^2 and serum potassium <5.0 mmol/L • Potassium binder can be used in CKD patients with hyperkalemia to allow optimal treatment with a RAS-blocker or an MRA to continue
ACC/AHA 2017[49]	<130/80 mm Hg in adults with hypertension and CKD	ACEIs or ARBs in hypertension and CKD (stage 3+ or stage 1–2 with albuminuria ≥300 mg/d)
Cardiac diseases (CAD/ACS)		
ESC 2024[46]	• Not CAD specific • SBP to 120–129 mm Hg, provided the treatment is well tolerated • Personalized and more lenient BP targets (e.g. <140 mm Hg) should be considered among patients meeting criteria: pretreatment symptomatic orthostatic hypotension, and/or age ≥85 years	BBs and RAAS blockers in patients with a history of MI BBs and/or CCBs in patients with symptomatic angina who require BP-lowering treatment

Contd…

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Guideline	*BP target*	*Management of hypertension*
ESH 2023[48]	The same treatment targets as in the general hypertensive population also applies to patients with CAD	• ACEIs (ARBs if not tolerated) or BBs are recommended • BBs and both DHP and non-DHP CCBs in patients with hypertension and CAD with angina pectoris • BB or non-DHP CCBs can be used to lower heart rate to 60–80 beats per minute in hypertensive patients with CAD
InSH 2023[1]	• <130/80 mm Hg • <140/80 in elderly patients	• ACE inhibitors/ARBs or BBs are advised • BBs and CCBs—both DHP and non-DHP for patients with hypertension and CAD with angina pectoris • BB or non-DHP CCBs can be used to lower heart rate to 60–80 beats per minute
ACC/AHA 2017[49]	<130/80 mm Hg is recommended in adults with SIHD and hypertension	• BBs, ACEIs, or ARBs as first-line therapy for compelling indications (e.g., previous MI, stable angina) in adults with SIHD and hypertension (BP ≥130/80 mm Hg) • Other drugs (e.g., DHP CCBs, thiazide diuretics, and/or MRAs) to be added as needed • DHP CCBs addition to BBs in adults with SIHD with angina and persistent uncontrolled hypertension • In adults who have had an MI or ACS, it is reasonable to continue BBs beyond 3 years as long-term therapy for hypertension • BBs and/or CCBs might be considered to control hypertension in patients with CAD (without HFrEF) who had an MI >3 years ago and have angina

ADA, American Diabetes Association; ESC, European Society of Cardiology; ESH, European Society of Hypertension; HFrEF, heart failure with reduced ejection fraction; InSH, Indian society of hypertension; KDIGO, kidney disease: improving global outcomes; RSSDI, Research Society for the Study of Diabetes in India; SIHD, stable ischemic heart disease

patients with proteinuric CKD, regardless of diabetic status.[25] While both drug classes are effective, ARBs often present a more favorable side-effect profile.[14,56] In nonproteinuric CKD, the benefit of RAAS inhibition remains debatable.[14]

Telmisartan: A Distinct Angiotensin II Receptor Blockers with Metabolic and Cardiovascular Advantages

Among ARBs, telmisartan offers unique benefits, extending beyond BP control. By activating peroxisome proliferator-activated receptor gamma (PPAR-γ), it enhances insulin sensitivity and glycemic control, making it especially effective in patients with T2DM or MetS, as supported by multiple studies (Table 3).[44,53,54]

Telmisartan offers strong CV protection, as demonstrated in the ONTARGET trial, in reducing CV risk in high-risk patients, making it a suitable alternative for those intolerant to ACE inhibitors (Table 3).[57] While the TRANSCEND trial did not show a significant reduction in the primary CV outcome, it did reveal modest benefits in secondary endpoints for patients with CVD or high-risk diabetes who could not tolerate ACEIs (Table 3).[58]

Real-world studies from India also confirm that telmisartan is effective for managing BP in those with essential hypertension and comorbid conditions, making it ideal for high-risk populations (Table 3).[55,59]

Together, these findings establish telmisartan as a well-rounded antihypertensive option that addresses BP, metabolic dysfunction, renal outcomes, and CV risk, making it especially valuable in patients with comorbidities.

Calcium Channel Blockers

Calcium channel blockers are a valuable first-line option for hypertension in patients with T2DM, MetS, or older individuals with isolated systolic hypertension, particularly for stroke prevention.[14] Both long-acting dihydropyridine (DHP) CCBs (e.g., amlodipine, nifedipine) and non-DHP CCBs (e.g., verapamil, diltiazem) do not exhibit negative metabolic effects and are suitable for T2DM.[44,53] However, CCBs, especially DHP types like amlodipine, are associated with a higher risk of HF and are less effective than RAAS blockers in preventing it.[14]

In CKD, DHP CCBs are effective for nonproteinuric cases but less so in proteinuric CKD, where RAAS blockade remains superior. Non-DHP CCBs may offer additional benefit by reducing proteinuria.[25]

Diuretics

Thiazide diuretics may negatively affect carbohydrate and lipid metabolism, although the data remain conflicting. Nonetheless, they are often essential in managing hypervolemia resulting from increased sodium and water reabsorption, with chlorthalidone and indapamide as preferred agents. Loop diuretics are not recommended because of their potential to impair glucose tolerance and contribute to hyperosmolar conditions, although the evidence in this regard is inconsistent.[60]

In CKD, diuretics help reduce fluid retention, arterial stiffness, and left ventricular mass index (LVMI). Thiazide-like diuretics are preferred for nonproteinuric CKD, while loop diuretics are more effective in advanced CKD with a lower eGFR. Combining loop and thiazide diuretics can be beneficial, but careful monitoring is essential to prevent excessive fluid loss.[60]

Thiazide diuretics are associated with reduced CVEs, as supported by trials like SHEP, MRC, and ALLHAT.[48,51] Loop diuretics are preferred to thiazides in ACS patients with HF or CKD with GFR <30 mL/minute because of superior efficacy in managing fluid overload.[51,52]

Beta-blockers

Beta-blockers (BBs) are generally not first-line agents for patients with diabetes or MetS due to adverse metabolic effects such as weight gain, dyslipidemia, and impaired insulin sensitivity. However, they may be used as add-on therapy when necessary.[5,14,53] When BBs are necessary, newer vasodilating options like carvedilol, nebivolol, and labetalol, or cardioselective agents such as bisoprolol and extended-release metoprolol succinate, are preferred to minimize these adverse effects. Carvedilol, in particular, offers additional benefits by reducing systemic peripheral resistance, enhancing glomerular filtration, and improving insulin sensitivity.[53]

In patients with CAD, BBs play a key role in hypertension and angina management and are recommended alongside DHP CCBs.[48] They should be prescribed post-MI unless contraindicated, as they improve prognosis. While their long-term benefit remains uncertain, therapy may be continued in the absence of contraindications. Cardioselective BBs like metoprolol and bisoprolol are preferred in CAD due to their heart rate—lowering effect, targeting around 70 bpm.[37]

Table 3: Studies on the efficacy and safety of telmisartan in managing hypertension with comorbid conditions

	Study 1[59]	*Study 2*[55]	*Study 3*[64]	*Study 4 (ONTARGET)*[57]	*Study 5 (TRANSCEND)*[58]	*Study 6*[54]	*Study 7*[65]
Year of study	2021	2018	2016	2008	2008	2005	2005
Study type	Retrospective real-world analysis	Retrospective observational	Prospective observational	RCT, double-blind	RCT, double-blind, placebo-controlled	RCT, double-blind, parallel-group	Prospective, multicenter
Population	1,304 Indian patients with essential hypertension and comorbidities	132 Indian patients with T2DM and stage I HTN	56 Indian CKD patients (96% hypertensive)	25,620 with vascular disease/ high-risk diabetes	5926 ACEI-intolerant patients	40 with MetS	92 hypertensive CKD patients with proteinuria
Intervention	Telmisartan mono- or +1 AHD class	Telmisartan 20–80 mg (mostly 40 mg)	Telmisartan	Telmisartan 80 mg vs ramipril 10 mg vs combination	Telmisartan 80 mg vs placebo	Telmisartan 80 mg vs losartan 50 mg	Telmisartan 40 → 80 mg (add-on)
Duration	1 month	12 weeks	3 months	Median 56 months	Median 56 months	3 months	6 months
Primary outcome	Change in SBP/DBP and goal achievement	BP and glucose control	Proteinuria, GFR, BP, safety	Composite CV events	Composite of CV death, MI, stroke, or hospitalization for HF	Insulin sensitivity, BP	BP reduction, proteinuria
BP reduction	Mean change of SBP/DBP with telmisartan monotherapy: 1. Essential hypertension and comorbid diabetes: –13.3/–7.3 mm Hg ($p < 0.001$) 2. Essential hypertension and comorbid dyslipidemia: –12.5/–8.8 mm Hg ($p < 0.001$) 3. Essential hypertension and comorbid CKD: –2.6/–3.6 mm Hg 4. Essential hypertension and comorbid CAD: –20.0/–10.4 mm Hg Mean change in SBP/DBP with telmisartan and 1AHD: 1. Essential hypertension and comorbid dyslipidemia: –10.8/–6.5 mm Hg ($p < 0.001$)	↓19.5–24.9 mm Hg SBP	↓8.9/4.7 mm Hg	↓0.9/0.6 mm Hg (telmisartan) ↓2.4/1.4 mm Hg (combination)	↓4.0/2.2 mm Hg	↓24h SBP/DBP vs losartan ($p < 0.05$)	↓19.6/11.8 mm Hg (office BP) ↓10–12/3–6 mm Hg (ABPM)
Metabolic effects	–	↓Postmeal glucose ($p = 0.046$)	–	–	–	↓FPG, insulin, HOMA-IR, HbA1c (telmisartan only)	–
Renal outcomes	–	–	Proteinuria ↓	–	–	–	Proteinuria ↓ (3.6–2.8 gm/24 hour, $p = 0.01$)
Adverse events	–	–	1 hyperkalemia case	Less cough/ angioedema; combination resulted in more adverse events	Fewer discontinuations; mild hypotension	–	5 discontinued, 2 hyperkalemia, 2 violations, 1 inefficacy
Conclusion	Effective BP control across mono- and add-on therapy; good for patients with comorbidities	Good BP and some glucose control	Significant renal and BP benefit	Telmisartan = ramipril in efficacy, fewer side effects. Combination = no added benefit	Well tolerated; modest CV benefit	Superior to losartan for BP and insulin sensitivity	Effective in reducing BP and proteinuria in CKD

ABPM, ambulatory blood pressure monitoring; AHD, antihypertensive drug; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; HOMA-IR, homeostatic model assessment of insulin resistance; HTN, hypertension; ONTARGET, ongoing telmisartan alone and in combination with ramipril global endpoint trial; TRANSCEND, telmisartan randomized assessment study in ACEI-intolerant subjects with cardiovascular disease

Table 4: SGLT2is impact on CV and renal outcomes

Trial	*Patients enrolled*	*eGFR inclusion criteria*	*Primary CV outcome*	*Renal outcome*
EMPA-REG OUTCOME[68]	7,020 T2DM patients, ≥18 years of age, BMI 45 kg/m^2	>30 mL/minute	14% reduction in major CVEs	46% reduction in composite renal endpoint [HR: 95% CI: 0.54 (0.40–0.75)]
CANVAS program[68]	10,142 patients with T2DM and high CV risk, 30% enrolled subjects had macro or microalbuminuria	>30 mL/minute/1.73 m^2	14% reduction in primary composite CV endpoint	40% reduction in hard renal outcomes [HR: 95%; CI: 0.60 (0.47–0.77)]; regression of albuminuria observed
DECLARE–TIMI 58[68]	17,160 patients with T2DM who had or were at risk for atherosclerotic CV disease	>60 mL/minute	Reduced CV death and HF hospitalizations, but no reduction in major CVEs	24% reduction in renal composite outcome [HR: 95% CI: 0.76 (0.67–0.87)]

BMI, body-mass index; CANVAS, canagliflozin cardiovascular assessment study; DECLARE–TIMI 58, dapagliflozin effect on cardiovascular events–thrombolysis in myocardial infarction 58; EMPA-REG OUTCOME, empagliflozin cardiovascular outcome event trial in type 2 diabetes mellitus patients

Mineralocorticoid Receptor Antagonists

Mineralocorticoid receptor antagonists, including spironolactone and eplerenone, are used in managing hypertension in diabetic patients.[5] Spironolactone is particularly effective at low doses. It reduces albuminuria and provides renoprotection independent of systemic hemodynamic changes.[6,14] However, potential side effects such as impotence, gynecomastia, type 4 renal tubular acidosis, and hyperkalemia limit its use.[6] Beyond diabetes, in CKD, MRAs improve BP control and cardiac function, though they increase hyperkalemia risk.[25,61]

Finerenone is a newer nonsteroidal MRA with higher specificity and fewer side effects. It has been approved by the FDA for reducing kidney function decline and CVEs in CKD patients with T2DM, as demonstrated in the FIDELIO-DKD and FIGARO-DKD trials.[61] The FIDELIO-DKD trial was conducted in 5,734 patients with CKD and T2DM. The primary composite endpoint, that is, kidney failure, ≥40% sustained decline in eGFR, or death from renal causes, occurred in 17.8% of the finerenone group vs 21.1% in the placebo group [hazard ratio (HR): 0.82; 95% confidence interval (CI): 0.73–0.93; $p = 0.001$], demonstrating a significant renal benefit. The incidence of the key secondary endpoint, a composite of CV death, nonfatal MI, nonfatal stroke, or HF hospitalization, was also lower in the finerenone group (13.0 vs 14.8%; HR: 0.86; 95% CI: 0.75–0.99; $p = 0.03$).[62]

Similarly, the FIGARO-DKD trial evaluated finerenone in 7,437 patients with CKD and T2DM over a median follow-up of 3.4 years. The primary composite outcome, that is, CV death, nonfatal MI, nonfatal stroke, or hospitalization for HF, occurred in 12.4% of the finerenone group vs 14.2% of the placebo group (HR: 0.87; 95% CI: 0.76–0.98; $p = 0.03$), mainly due to fewer hospitalizations for HF (HR: 0.71; 95% CI: 0.56–0.90). The secondary kidney outcome occurred in 9.5% of finerenone-treated patients vs 10.8% in the placebo group (HR: 0.87; 95% CI: 0.76–1.01), showing a nonsignificant trend toward renal benefit.[63]

Sodium-glucose Cotransporter 2 Inhibitors

Sodium-glucose cotransporter 2 inhibitors (SGLT2is) are primarily known for their glucose-lowering and CV benefits, but they also demonstrate significant BP-lowering effects.[64–66] In a study, empagliflozin 10 mg reduced SBP by 3.4 mm Hg from a baseline of 131.34 mm Hg ($p < 0.001$), while the 25 mg dose reduced SBP by 4.1 mm Hg from baseline SBP of 131.18 mm Hg ($p < 0.001$). In another study, empagliflozin led to an 8.39 mm Hg BP reduction over 24 weeks ($p = 0.0025$).[64] Similarly, dapagliflozin lowered SBP by 4.28 mm Hg more than placebo in one study ($p = 0.0002$), highlighting its antihypertensive potential.[64]

A *post hoc* analysis of the CREDENCE trial highlighted a high prevalence of hypertension, with SGLT2is consistently lowering BP by 3.5 mm Hg from baseline within 3 weeks and maintaining this effect over time.[64]

Additionally, SGLT2is have been evaluated in randomized controlled trials (RCTs) with CVEs as the primary outcome (Table 4). Subsequently, their secondary analyses were the first to reveal the protective effect of these inhibitors against CKD progression.[43]

Potassium Binders

Novel potassium binders like patiromer and sodium zirconium cyclosilicate have demonstrated efficacy in normalizing and maintaining serum potassium levels in CKD patients treated with ACE inhibitors, ARBs, or spironolactone while being well tolerated. Therefore, they help to maintain serum potassium below 5.5 mmol/L, enabling continued optimal treatment with renin–angiotensin system (RAS) blockers or MRAs.[60]

Other Drugs

Other antihypertensive classes, alpha-blockers and centrally acting agents, can aid in BP control for CKD patients with resistant hypertension. Direct vasodilators like hydralazine and minoxidil should be used cautiously, as these may lead to substantial fluid retention and reflex sympathetic activation, resulting in tachycardia.[60]

Combination Therapy

Over two-thirds of hypertensive individuals do not achieve control with monotherapy.[14] Monotherapy is only indicated for low-risk patients with BP levels of 140–159/90–99 mm Hg or in elderly (>80 years) or frail individuals.[53] For most patients, hypertension management should commence with combination therapy.[53] Guidelines recommend initiating a combination of a RAAS blocker and CCB or a diuretic.[53] This strategy is supported by robust clinical trial evidence.

The ASCOT-BPLA trial demonstrated that amlodipine reduced stroke, CVEs, and all-cause mortality more effectively than atenolol in patients with untreated or uncontrolled hypertension and at least three additional CV risk factors.[14] Similarly, the ACCOMPLISH trial indicated that benazepril with amlodipine was more effective than benazepril with hydrochlorothiazide in reducing CVEs (9.6 vs 11.8%; HR: 0.80; $p < 0.001$) for initial management in patients with increased CV risk.[14,67] Similarly, telmisartan and amlodipine combination has been proven effective and well tolerated in hypertensive patients with added risks.[68]

Beyond CV protection, renoprotective effects of combination therapy have been reinforced by trials like Bergamo Nephrologic Diabetes Complications Trial (BENEDICT) and Action in Diabetes and Vascular Disease (ADVANCE). BENEDICT showed that trandolapril + verapamil significantly reduced progression from normoalbuminuria to

microalbuminuria in T2DM patients compared to trandolapril alone. Similarly, the ADVANCE trial demonstrated that perindopril and indapamide combination slowed progression from normoalbuminuria to microalbuminuria over 4.3 years of follow-up.[69]

Evidence from studies indicates that combining cilnidipine with RAS inhibitors offers added renal protection in CKD over RAS inhibitors alone.[70,71] The CARTER study demonstrated that cilnidipine was superior to amlodipine in decreasing UACR at 12 months (cilnidipine group −14.4% vs amlodipine group +13.9%, $p < 0.01$) when added with RAS inhibitor. Similar effect of cilnidipine in reducing proteinuria has been reported in other studies.[71]

Patients with MetS often exhibit resistance to monotherapy, necessitating early use of combination treatment.[53] Among ARB-based combinations, telmisartan plus amlodipine has shown strong efficacy in 64 hypertensive MetS patients, with 95.3% achieving BP control. LVMI and microalbuminuria significantly decreased, and diastolic function improved. These findings highlight the antihypertensive, nephroprotective, and cardioprotective benefits of combination therapy in high-risk individuals with MetS.[72]

Consensus Statements

Based on the discussion of experts after considering the evidence, the following agreement was reached for the following consensus statements.

Statements	*Average of a total of responses (A + B)*
A treatment goal of BP <130/80 mm Hg can be considered in hypertensive subjects with MetS	90%
In patients with MI, other ACS, or stroke, the targets should be <130/80 mm Hg for office BP and <125/75 mm Hg for home BP	93%
In patients with HF or CKD, the targets should be <130/80 mm Hg for office BP and <125/75 mm Hg for home BP	90%
Telmisartan is the preferred ARB for the management of hypertension with MetS, considering its proven efficacy in reducing BP, as well as urine protein levels, the risk of ESRD, and progression of nephropathy	91%
BP control is difficult in diabetes, and combination treatment is almost always necessary	88%
Telmisartan and its combinations should be recommended as first-line treatment (when combination therapy is recommended) for patients with hypertension with MetS	92%
Regardless of the presence or absence of T2DM or hypertension, albuminuria should be treated as early as possible, considering the significant and continuous association between the degree of albuminuria and the subsequent risks of major CV events	90%
SGLT2is are recommended for patients with diabetic and nondiabetic nephropathies associated with CKD if eGFR is at least 20 or 25 mL/minute/1.73^2	86%
In patients with a history of MI who require BP-lowering treatment, BBs, and RAS blockers are recommended as first line of treatment	92%
BBs should be used for 3 years in patients with HT with ACS	77%

Conclusion

Achieving optimal BP control is crucial, especially in Indian patients with hypertension complicated by comorbidities such as MetS, CAD, CKD, or diabetes. Hypertension in these conditions not only increases CV and renal risks but also complicates disease management, making strict BP control essential. Given the rising burden of hypertension and diabetes in India, along with high rates of uncontrolled BP, a target of <130/80 mm Hg is generally recommended, with more stringent home BP targets for high-risk individuals.

Telmisartan is preferred for managing hypertension in MetS due to its beneficial effects on BP, proteinuria, and kidney disease progression. Considering the high prevalence of diabetic kidney disease in India, early intervention with telmisartan and SGLT2is can help slow CKD progression. Additionally, early treatment of albuminuria is essential, regardless of diabetes or hypertension status, due to its strong link with CV risks. Furthermore, ARBs with BBs or diuretics are better choices of drugs in hypertensive patients with CAD.

Innovative treatment modalities are increasingly being explored to address the complexities of hypertension. Fixed-dose combination pills are being increasingly adopted to enhance medication adherence and simplify treatment regimens. Nonsteroidal MRAs provide safer alternatives for patients with complications such as HF or CKD. Experimental approaches, including angiotensin-targeting vaccines, are also under development and may provide long-term BP control in the future.

Moreover, integrating digital health technologies, such as wearable devices, mobile health applications, and remote monitoring tools, can significantly enhance patient engagement and enable timely clinical interventions, thereby improving the overall management of hypertension and its comorbidities in the Indian context.

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