Hypertension: The Silent Killer Unvalid – Areview Of Risk Factors and Prevention

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***Abstract*- Hypertension is the most common modifiable risk factor for death and disability. Stroke, heart failure, accelerated systemic and coronary atherosclerosis, chronic renal disease, decreasing blood pressure with antihypertensive drugs, lowering the prevalence of cardiovascular disease, and damage to target organs are further modifiable risk factors. According to the 2017 American Heart Association (AHA)/American College of Cardiology (ACC) recommendations, hypertension is defined as having a diastolic blood pressure of at least 80 mmHg or a systolic blood pressure of at least 130 mmHg. Blood pressure should be less than 130/80 mmHg in patients with CHD, CHF, diabetes mellitus, post-renal transplantation, and stroke. Reducing the quantity of salt in the diet, helping the patient shed excess weight, getting regular exercise, drinking moderation, and increasing consumption of foods high in potassium were some of the recommended lifestyle modifications. First-line antihypertensive medications should usually include ARBs, calcium channel blockers, ACE inhibitors, thiazide diuretics, and other medications that have been shown to reduce cardiovascular events. Two interventional strategies used in clinical practice to treat different types of treatment-resistant hypertension are baroreflex activation therapy and renal denervation. Carotid body ablation and AVF implantation are two additional interventional techniques that can stop the progression of cardiovascular disease or the death of a hypertensive patient.**

***Keywords*- Carotid body ablation therapy, antihypertensive medication therapy, target blood pressure, and renal denervation.**

1.INTRODUCTION

Hypertension is defined as elevation of the systolic, diastolic, or both above normal levels; it is common in both developed and developing countries and becomes more common with age. Although in recent years the standard for hypertension has been a blood pressure reading of 140/90 mmHg or higher, the 2017 American College of Cardiology-A lower cutoff point of 130 systolic blood pressure was established as the definition of hypertension by the American Heart Association's (ACC-AHA) Hypertension Guideline.80 mmHg or more during the diastolic phase of blood pressure [1]. The 2017 ACC/AHA guideline definition (BP ≥ 130/80 mmHg) places the overall prevalence of hypertension among adults in the United States at 45.6%, compared to the previous definition's 31.9% [2]. In contrast, the rate of hypertension control among treated patients was 46.6% at a target of less than 130/80 mmHg, but 61.0% at a target of less than 140/90 mmHg [10].

Hypertension is the most important and controllable risk factor for adult mortality and CV events worldwide [3,4]. Adults who experience their first MI at 69% [5], their first stroke at 77% [4], their first HF at 74%, and their first PAD at 60% [5] all have hypertension. Furthermore, hypertension significantly increases the risk of developing dissecting aortic aneurysms, angina pectoris, LVH, thoracic and abdominal aortic aneurysms, CKD, atrial fibrillation, diabetes mellitus, vascular dementia, and ophthalmologic diseases [6]. Treatment with antihypertensive medications, which lower blood pressure and related target organ damage, can significantly reduce the increased risk associated with elevated blood pressure. 69 medications from 15 classes—many of which are also sold as single pills—have been approved for the treatment of hypertension in the United States. Despite these treatment options, 10% to 15% of general RH is considered uncontrolled blood pressure on ≥3 antihypertensive medications of different classes, at optimal doses, or requiring ≥4 medication to control blood pressure [7,8]. Hyperaldosteronism, vascular disease, Cushing syndrome, and pheochromocytoma are the main causes of RH. About 0.5% of hypertensive patients have resistant hypertension, which is defined as uncontrolled blood pressure on at least five medications [9]. Recent drug monitoring studies have shown that between 25% and 65% of patients with apparent TRH did not comply with BP-lowering therapy [10,11,12,13]. Despite being prescribed three to five antihypertensive medications, blood or urine samples from 24% to 34.5% of these patients had no indication of taking antihypertensive medication.

In 123 randomized trials of antihypertensive medication therapy, 16,000 participants were found, according to a systematic review and meta-analysis [14]. According to the review, major CV events were significantly reduced by 20%, CHD by 17%, stroke by 27%, and HF by 28% for every 10 mm Hg drop in SBP. In all populations analyzed, this resulted in a 13% drop in all causes of death [14]. 9361 adults were randomly assigned to have a systolic blood pressure goal of less than 120 mm Hg or less than 140 mm Hg as part of the SPRINT (systolic blood pressure intervention trial) [15]. The average age of these patients is 67.9 years, and they have a high CV risk and systolic blood pressure of 130 to 180 mm Hg. Additionally, they do not have an estimated glomerular filtration rate of less than 20 ml/min/1.73 m2, diabetes mellitus, a history of stroke, or asymptomatic heart failure within the last six months [11]. At 3.26 years of follow-up, there had been a 25% reduction in the primary composite

outcome of MI, stroke, HF, or death from CV causes; there had also been a 27% reduction in all cause's mortality, a 38% reduction in HF, a 43% reduction in CV death, and a 22% reduction in primary composite outcome or death [16].

2.Blood Pressure Targets Recommended by Different Guidelines

Adults over 60 should have their blood pressure lowered to less than 150/90 mmHg if they do not have diabetes mellitus or chronic kidney disease, and less than 140/90 mmHg if they do, per the 2013 Eight Joint National Committee (JNC 8) guidelines for managing hypertension [16]. A blood pressure of less than 140/90 mmHg is the goal for adults with hypertension who are under 80 years old and do not have diabetes mellitus or chronic kidney disease (CKD), according to the minority opinion from JNC 8 [17]. The National Institute of Health and Care Excellence (NICE) in the United Kingdom updated its hypertension guideline in 2013, recommending that blood pressure be lowered to less than 140/90 mmHg in individuals under 80 years of age [18]. According to the guidelines, blood pressure in adults over 80 should be lowered to less than 150/90 mmHg [18]. The 2014 International Society of Hypertension (ISH) guidelines recommended lowering blood pressure to less than 140/90 mmHg in adults over the age of 80 [19]. Furthermore, according to these guidelines, blood pressure in adults over 80 years of age with a blood pressure ≥ 150/90 mmHg should be lowered to <150/90 mmHg, unless they have diabetes mellitus (DM) or chronic kidney disease (CKD), in which case a target goal of <140/90 mmHg should be considered [1].

The American College of Cardiology, the American Heart Association, and the American Society of Hypertension published guidelines in 2015 on the treatment of hypertension in patients with CHD [20]. The target blood pressure for adults with CHD and ACS should be less than 140/90 mmHg if they are under 80 years old, but more than 150/90 mmHg if they are older. These guidelines state that blood pressure should be lowered to less than 130/80 mmHg in adults with CHD who have had a MI, stroke, TIA, carotid artery disease, or abdominal aortic aneurysm. The National Heart Foundation (NHF) of Australia published guidelines on hypertension in 2016 that state that patients with uncomplicated hypertension should aim for a blood pressure of 140/90 mmHg or lower [21]. Attaining a systolic blood pressure target of less than 120 mmHg can improve cardiovascular health in an individual [21]. These adults ought to have been closely watched to identify treatment-related side effects like hypotension, syncope, electrolyte imbalance, and acute kidney injury [20].

The 2017 American College of Physicians (ACP)/American Academy of Family Physicians (AAFP) hypertension guidelines include three recommendations [22].

I. Adults 60 years of age or older with systolic blood pressure greater than 150 mmHg should have their systolic blood pressure lowered to less than 150 mmHg in order to reduce the risk of death, stroke, and cardiovascular events.
II. Adults 60 years of age or older who have had a stroke or transient ischemic attack should have a systolic blood pressure of less than 140 mmHg in order to reduce the risk of having another stroke.
III. Adults over 60 who are deemed to have a high cardiovascular risk should have their target systolic blood pressure lowered to less than 140 mmHg in order to reduce their risk of stroke and cardiovascular events.

According to the 2017 ACC/AHA hypertension guidelines, <120/80 mmHg is considered normal blood pressure, as shown in Table 1 [23]. Elevated blood pressure was defined as readings between 120 and 129 mmHg at the systolic level and under 80 mmHg at the diastolic level. For this condition, treatment with a lifestyle measurement [24]. Stage one is systolic hypertension. Stage 2 hypertension is defined as a systolic blood pressure of 140 mmHg or a diastolic blood pressure of 80–89 mmHg.The diastolic blood pressure is 90 mmHg.

For the secondary prevention of recurrent cardiovascular events in adults with clinical cardiovascular disease, such as CHD, CHF, and stroke, and an average blood pressure of at least 130 mmHg or 80 mmHg, the 2017 ACC/AHA hypertension guideline recommended lifestyle changes in addition to blood pressure medications [25,26]. For the primary prevention of CV disease in adults with an estimated 10% 10-year risk of atherosclerotic CVD (ASCVD) and an average systolic or diastolic blood pressure of ≥130 mmHg or ≥80 mmHg, these guidelines suggested BP-lowering medication in addition to lifestyle modifications. [28,29]. For primary CV prevention, these guidelines recommended BP-lowering medication along with lifestyle modifications for adults with an average systolic blood pressure of ≥140 mmHg or an average diastolic blood pressure of ≥90 mmHg [30] and an estimated 10-year risk of ASCVD< 10%.

The 2017 ACC/AHA hypertension guidelines recommended lowering blood pressure in adults with CHD to less than 130/80 mmHg. a person suffering from a Lacunars stroke, PAD, diabetes mellitus [29], reduced left ventricular ejection fraction in CHF, preserved left ventricular ejection fraction in CHF [30], and chronic kidney disease [1], after a kidney transplant [11], for the secondary prevention of stroke and for adults 65 years of age or older who live in an ambulatory community [28].

3.Evaluation of the Individual

The first step is to confirm the diagnosis of hypertension. It was advised to take a blood pressure reading using a standardized technique, dependable equipment, and a cuff that was the right size at least twice [1]. The 2017 ACC/AHA hypertension guideline recommended ambulatory blood pressure monitoring or home blood pressure monitoring for the diagnosis of white coat hypertension or masked hypertension [1]. White coat hypertension is the term for blood pressure that is elevated in a hospital or clinic but stays normal at home or when using an ambulatory blood pressure monitoring device. Masked hypertension is the term for blood pressure that is normal in a hospital or clinic but elevated at home or when using an ambulatory blood pressure monitoring device.

Table 1. Classification of BP in adult according to ACC/AHA 2017 hypertension guidelines [23]

Blood pressure category	Definition
Normal BP	Systolic BP < 120 mmHg and diastolic BP < 80 mm Hg.
Elevated BP	Systolic BP 120 - 129 mmHg and diastolic BP < 80 mm Hg.
Hypertension:	
Stage-1	Systolic BP 130 - 139 mmHg and diastolic BP 80 - 89 mm Hg.
Stage-2	Systolic BP ≥ 140 mmHg and diastolic BP ≥ 90 mm Hg.

Note: BP: Blood pressure.

Ambulatory blood pressure monitoring allows blood pressure to be taken while a patient goes about their daily activities. It also allows blood pressure to be measured both during the day and at night, allowing for the identification of symptomatic hypotension [1]. A complete medical history should be obtained as soon as the diagnosis is made in order to assess any coexisting conditions and risk factors for the condition, including lifestyle decisions, cardiovascular disease risk factors, and characteristics that might point to secondary causes of hypertension. Examining for bruits in the femur, abdomen, or carotid arteries increases the risk of renal artery stenosis. Elevated blood pressure in the arms and legs or decreased femoral pulses are indicators of aortic coarctation or severe aortoiliac disease. Cushing disease can be identified by the presence of interscapular fat deposition, moon faces, or abdominal striae. Primary hypertension is defined as a steady rise in blood pressure associated with weight gain and a positive family history. Conversely, secondary hypertension is indicated by multiple or decreased heart rate in addition to damage to target organs; Table 2 lists the common causes of secondary hypertension. As shown in Table 3, the initial laboratory examination should look for coexisting conditions and target organ damage that may affect how the patient responds to medication.

Table 2. Common causes of secondary hypertension [8].

Following are the common causes of secondary hypertension

- Renovascular disease.
- Coarcation of the Aorta.
- Pheochromocytoma.
- Chronic kidney disease.
- Cushing syndrome.
- Primary hyperaldosteronism.
- Thyroid disease.
- Obstructive sleep apnea.
- Congenital adrenal hyperplasia.

Table 3. Basic investigation of hypertension

Following are the basic investigation of hypertension:

- Complete blood count-TLC, DLC, Hb %, RBC
- Renal function test-Blood urea, serum creatinine, potassium, Sodium, calcium, uric acid
- Blood sugar level
- Urinalysis
- Lipid profile
- Thyroid function test
- Electrocardiography
- Urine albumin to creatinine ratio
- Measure plasma aldosterone/Renin ratio
- Measurement of 24 hours urinary meta nephrons.

The aldosterone/renin ratio is a useful screening method for primary aldosteronism [3]. Urine can be collected for 24 hours following the patient's regular diet in order to measure creatinine clearance, estimate the amount of sodium and potassium consumed through diet, and measure aldosterone excretion. For patients who may have pheochromocytoma, measuring the 24-hour urine or plasma meta nephrons is a helpful screening technique [4]. Patients in whom suspicion of renal artery stenosis is raised should not undergo imaging. Resistant hypertension is linked to increased 24-hour urine albumin excretion and left ventricular mass index in terms of target organ damage [2].

4.Controlling High Blood Pressure

Treatment options for hypertension include both pharmacological and nonpharmacologic approaches. Whether or not pre-existing CV, DM, and CKD are taken into consideration when choosing a course of treatment. The 2017 AHA/ACC guideline states that patients without these conditions who have stage 1 hypertension should have their 10-year risk of cardiovascular disease estimated. If the risk is less than 10%, it makes sense to try lifestyle modification alone for three to six months. For patients with pre-existing conditions such as diabetes mellitus, chronic kidney disease, and a 10-year risk of cardiovascular events of 10% or higher, medication and lifestyle modification are recommended for stage 2 hypertension.

4.1. Interventions Not Medicinal

The following is a list of non-pharmacologic methods for treating hypertension.

4.1.1. Dietary Salt Limitation

Less than 1500 mg of sodium should be consumed daily. Patients with general hypertension have been demonstrated to benefit from dietary salt reductions, with systolic and diastolic blood pressure reductions of 5 to 10 mmHg and 2 to 6 mmHg, respectively.

4.1.2. Loss of Weight If a patient is overweight or obese

losing weight can help lower blood pressure and cut down on the amount of prescription medications they need to take [4]. A 10 kg weight loss is associated with an average reduction in systolic blood pressure of 6 mmHg and diastolic blood pressure of 4.6 mmHg, according to studies on long-term weight loss.

4.1.3. Participation in Movement

Frequent aerobic exercise reduced blood pressure by an average of 4 mmHg in the systolic and 3 mmHg in the diastolic range. Consequently, it is recommended that patients perform 90–150 minutes of resistance or aerobic training each week [4]. As a result, it is recommended that all patients with hypertension exercise.

4.1.4. Moderate Intake of Alcohol

All hypertension patients can benefit from moderate alcohol consumption (≤ 2 drinks per day for men and ≤ 1 drink per woman) as it can reduce blood pressure by 3 to 8 mmHg in the systolic and 1 to 4 mmHg in the diastolic ranges [1].

4.1.5. A high-fiber, low-fat diet

A dietary strategy to stop smoking is to consume a diet high in fruits and vegetables, low in saturated fat, and high in potassium, magnesium, and calcium. A patient with hypertension saws a 11.4 systolic drop in blood pressure with DASH mmHg and 5.5 mmHg lower in the blood pressure diastolic range [2]. An abundance of fruit and Eating vegetables lowers blood pressure and improves endothelial function.

4.1.6. Drugs used as contraceptives are eliminated

If avoiding medication entirely is not an option, then the lowest dosage that works best should be taken. The primary drugs that can obstruct the regulation of blood pressure are NSAIDS.

Blood pressure should be regularly monitored when using these medications to treat hypertension, as the antihypertensive regimen may need to be adjusted. When treating hypertension, the following drugs ought to be avoided [11].

4.2. Pharmacological Therapy

The 2017 ACC/AHA guideline, which recommended beginning antihypertensive medication treatment with two first-line drugs from different classes, either separately or in a fixed dose combination [1], stated that the target blood pressure should be less than 130/80 mmHg.

INITIAL DRUG SELECTION:

The four classes of antihypertensive medications from which the first agent can be selected are ACE inhibitors, thiazide type diuretics, angiotensin receptor blockers, and calcium channel blockers] [5]. With the exception of the main effect that beta blockers given after MI reduced CAD event and calcium channel blockers reduced stroke, a meta-analysis of 147 randomized controlled trials involving 464,000 hypertensive patients revealed that all major antihypertensive drug classes (diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, and calcium channel blockers) cause reduction in CAD event and stroke for reduction in blood pressure [15]. Cost, tolerability, effectiveness, and the presence of specific comorbidities are all factors that should be taken into consideration when choosing an antihypertensive medication to treat adult hypertension, according to the 2011 ACC/AHA hypertension guidelines [6].

Table 4. Medicines avoided during treatment of hypertension [2].

Following are the medicines during treatment of hypertension:

- Non-steroidal anti-inflammatory drugs
- Oral contraceptives pills
- Corticosteroids
- Tricycle antidepressant drugs
- Monoamine oxidase inhibitors

The 2011 ACC/AHA hypertension guidelines state that elderly patients with primary hypertension may be treated with beta blockers, ACE inhibitors, diuretics, ARBs, and calcium channel blockers (CCBs) [6].

Diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and calcium channel blockers are recommended treatments for non-Black adults with primary hypertension, per the 2013 JNC 8 guidelines for the management of hypertension [16].

Angiotensin receptor blockers (ARBs) or angiotensin converting enzyme inhibitors (ACE inhibitors) should be used to treat primary hypertension in adults who are not black and who are older than 60, according to the 2014 American Society of Hypertension (ASH)/International Society of Hypertension (ISH) guideline [19].

These recommendations state that adults with primary hypertension who are not black and who are at least 60 years old should be treated with diuretics, CCBs, ACE inhibitors, or ARBs [9]. These guidelines recommended treating black adults with primary hypertension with thiazide diuretics or calcium channel blockers [19].

The following is stated in the 2017 American College of Cardiology (ACC)/American Heart Association (AHA) hypertension guidelines [1] regarding antihypertensive medication treatment for primary and secondary hypertension:

4.2.1. White and non-Black people with primary hypertension

If a patient is under 60 years old, antihypertensive medications should begin with ACE inhibitors or ARBs, followed by calcium channel blockers or diuretics. If a third medication is required, ACE inhibitors or ARBs along with calcium channel blockers and thiazide diuretics are administered [19].

4.2.2. White and non-Black Individuals with Primary Hypertension

ACE inhibitors, also known as ARBs, are the preferred antihypertensive medications. If the patient is over 60, thiazide diuretics, also known as CCBs, should be taken next. If thiazide diuretics, CCB, ACE inhibitors, OR ARB are required as a third antihypertensive medication, they ought to be combined (1).

4.2.3 Primary Hypertension in African Americans

If a third antihypertensive drug is needed, CCBs, ACE inhibitors, ARBs, or thiazide diuretics should be given in combination. Thiazide diuretics, or CCBs, should be prescribed as the first antihypertensive drug.

4.2.4. Stable Coronary Heart Disease and Hypertension

Patients with stable CAD and hypertension are treated with beta blockers plus ACE inhibitors or ARBs; if a third antihypertensive drug is needed, a combination of beta blockers plus ACE inhibitors or ARB plus thiazide diuretics or CCBs should be administered.

4.2.5 Heart Failure Associated with Reduced Left Ventricular Ejection Fraction and Hypertension

ARBs, diuretics, and ACE inhibitors are used in conjunction with beta blockers (carvedilol, metoprolol, and bisoprolol) to treat patients with heart failure (HF) who have hypertension and a decreased left ventricular ejection fraction.

4.2.6. Preservation of Left Ventricular Ejection Fraction in Heart Failure

Heart failure and preserved left ventricular ejection fraction in a hypertensive patient should have volume over load and be treated with diuretics and hypertension given with beta blockers plus ACE inhibitors or ARSs plus mineralocorticoids antagonistic receptors [30].

4.2.7. Heart Failure (connected to kidney disease (chronic))

In order to slow the progression of the disease, ACE inhibitors should be used to treat patients with hypertension and CKD stage 3 or higher, as well as stage 1 or stage 2 with albuminuria ≥ 300 mg/day. If ACE inhibitors are not tolerated by the patient, ARBs should be used [1]. Adults with stage 1 or stage 2 CKD without albuminuria should be treated with first-line antihypertensive drugs [1].

Gives ACE inhibitors or, in the event that three antihypertensive medications are needed, ARB plus thiazide diuretic plus CCBs. In order to improve glomerular filtration rate and kidney survival after kidney transplantation, CCAs are used to treat hypertension [1].

4.2.8. A brief ischemic attack or stroke combined with elevated blood pressure

ACE inhibitors, ARBs, or thiazide diuretics should be used to treat hypertensive patients who have experienced a transient ischemic attack or stroke. If ACE inhibitors or thiazide diuretics plus ARBs or CCBs are needed as a third antihypertensive drug, they should be added.

4.2.9. Peripheral Arterial Disease and Hypertension

Patients with PAD and hypertension should be treated with any of the first-line antihypertensive drugs, including beta blockers, ACE inhibitors, ARBs, CCBs, and diuretics, just like patients without peripheral arterial disease.

4.2.10. Hypertension and Diabetes Mellitus

Patients with diabetes mellitus and hypertension should be treated with ACE inhibitors, ARBs, CCBs, and thiazide diuretics. The first line of treatment for patients with diabetes mellitus, hypertension, and persistent albuminuria should be ACE inhibitors or ARBs.

4.2.11. Thoracic Aortic Aneurysm and Hypertension

Beta blockers are the suggested antihypertensive drug for patients with hypertension and thoracic aortic aneurysm [25]. Beta blockers have also been connected to better and increased survival in aortic dissection.

4.2.12 Hypertension and Pregnancy

ARBs, ACE inhibitors, direct renin inhibitors, and atenolol shouldn't be taken by pregnant women who have hypertension. Medetol, hydralazine, nifedipine, and labetalol are the suggested drug combinations for pregnant patients with hypertension.

4.2.13 Hypertension Resistant

Treatments for obesity and other comorbidities, identification and management of secondary hypertension, and lifestyle changes were employed to treat RH [1]. Need to If a fourth antihypertensive drug is unable to lower blood pressure, then administer Spironolactone is a medicinal agent that functions as an antagonist of mineral corticoids receptors.

5. An Intriguing Approach to Treating Hypertension

Section 1: Innovative Drugs for the Treatment of Hypertension

5.1.1. Aldosterone-Releasing Agent

The mineralocorticoid aldosterone regulates the water and electrolyte balance of the body. Elevated aldosterone levels have been linked to the development of hypertension as well as other disorders like heart failure, myocardial fibrosis, and hypertrophy. Aldosterone acts on the mineralocorticoid receptor in the cortical collecting duct of the nephron, resulting in a volume-expanded form of hypertension. Mineralocorticoid receptors increase potassium loss and sodium and water reabsorption by stimulating the expression of sodium channels. In the zonaglomerulosa of the adrenal cortex, 11-deoxycorticosterone is converted to testosterone by the mitochondrial cytochrome P450 enzyme aldosterone synthase, which is encoded by the CYP11B2 gene [8].

Mineralocorticoid Receptor Antagonists

An adjuvant treatment for patients with RH has been spironolactone monotherapy, a mineralocorticoid receptor antagonist that has been demonstrated to have a slight lowering effect on blood pressure. Spiro lactone has not been used as much because of its lack of selectivity for the mineralocorticoid receptor at higher doses, which results in strong progestogenic and antiandrogenic activity that causes negative effects in both men and women due to its structural similarity to progesterone. The antiandrogenic effects of spironolactone are absent from plenone, a more selective mineralocorticoid receptor antagonist. However, due to its short half-life (3–4 hours), plenone is less effective and requires a twice-daily dosage due to its decreased antihypertensive efficacy. The dihydropyridine compound's MRA activity was optimized, leading to the creation of finerenone, also known as BAY 94-886. This nonsteroidal MRA does not affect the L-type calcium channel and has a higher affinity than eplerenone for the MR. It is also more selective for the MR than other steroid hormone receptors. Finerenone preserves the sodium-potassium balance of the kidneys while enhancing cardiac activity and cardiac function. In a preclinical model of heart failure and renal dysfunction associated with hypertension, finerenone provided greater protection to the heart and kidneys than steroidal mineralocorticoid receptor antagonists.

The first orally active aldosterone synthase inhibitors are LCI699, an aldosterone synthase inhibitor. In animal models of heart failure and hypertension, they have been demonstrated to lower urine and plasma aldosterone concentrations, raise plasma renin activity, and shield organs from harm. Similar effects on aldosterone and renin levels have also been reported in healthy humans [7] and hypertensive patients. The first randomized, double-blind, placebo-controlled trial of LCI699 involved 524 patients with primary hypertension and assessed the safety and efficacy of different doses of LCI699 in conjunction with eplerenone [9]. All doses of LCI699 resulted in a significant reduction in office systolic blood pressure; these reductions were comparable to those caused by eplerenone. While eplerenone increased plasma aldosterone levels, LCI699 decreased them; both drugs were well tolerated.

5.1.2. Vasopeptidase Inhibitors

Neprilysin, a zinc metalloprotease, is a therapeutic target for hypertension and other cardiovascular diseases because it breaks down the natriuretic peptides atrial natriuretic peptide (ANP), B type natriuretic peptide (BNP), and urodilatin. In addition, natriuresis, vasodilatation, inhibition of the renin-Angiotensin-aldosterone system, decreased sympathetic drive, and antiproliferative and antihypertrophic effects on the heart are caused by an increase in circulating natriuretic peptide levels brought on by Neprilysin inhibition.

The Natriuretic Peptide Receptor's Opponent

Natriuretic peptide receptor agonists are being developed as an alternative to blocking the breakdown of endogenous natriuretic peptides for the treatment of heart failure and refractory hypotension. The synthetic natriuretic peptide receptor A (NPR-A) agonist PL-3994 has a prolonged half-life after subcutaneous administration due to its reduced affinity for the natriuretic peptide clearance receptor (NPR-C) and increased resistance to Neprilysin [1]. A mimic of an amino acid is also present. In a phase I study with healthy participants, a single subcutaneous dose of PL-3994 caused greater diuresis and natriuresis as well as a reduction in systemic blood pressure when compared to a placebo. In a phase II study, participants with hypertension taking at least one antihypertensive medication demonstrated a drop-in mean systemic blood pressure relative to a placebo. Particularly PL-3994 appeared to complement ACE inhibitors, suggesting that it could be added to conventional care for patients with refractory or RH or HF.

5.1.3. Dopamine hydroxylase inhibitor

Dopamine β-hydroxylase, the enzyme that catalyzes the hydroxylation of dopamine to form noradrenaline in the sympathetic nervous system, is one possible therapeutic target for the treatment of hypertension and other cardiovascular disorders marked by sympathetic activation in heart failure. In theory, there is a benefit to inhibiting dopamine β-hydroxylase rather than blocking adrenergic receptors: Initially, it causes the sympathetic nervous system to gradually slow down. Second, it increases dopamine availability, which results in renal vasodilatation, natriuresis, and diuresis. First, second, and early third generation DβH inhibitors, such as disulfiram, fusaric acid, and nepicastat, were not clinically useful due to either lack of potency or selectivity for DβH or serious adverse effects related to the central nervous system. Since it does not cross blood brain barriers, etamicastat, when taken orally, is a strong and reversible inhibitor of dopamine β-hydroxylase that is specific for peripheral Dopamine β-hydroxylase. Studies on men with mild to moderate hypertension and those in excellent health showed significant dose-dependent declines in 24-hour ambulatory BP.

5.2. Section 2: Interventional Approach to the Management of Hypertension

In the management of arterial hypertension, interventional strategies are mentioned as a therapeutic option for treating various hypertensions that do not respond to treatment.

5.2.1. Decrease in Renal Capacity

This rapidly developing field of study has seen the publication of numerous papers pertaining to RDN. Increased sympathetic activity affects arterial hypertension's onset, maintenance, and acceleration [6]. Blood volume and blood pressure rise when the kidney's efferent sympathetic nerve is activated because it increases renin release, enhances tubular reabsorption of water and sodium, and decreases renal blood flow. The primary objective of treatment for essential hypertension is to prevent the activation of the renal sympathetic outflow by lowering blood pressure through endovascular procedures. Catheter-based renal denervation is a novel interventional strategy that specifically targets the sympathetic nerve activity. The evaluation of renal sympathetic nerve ablation using a radiofrequency catheter has been met with great enthusiasm.

Four ablations can be performed for each renal artery in a single, quick treatment session using the current multielectrode denervation system, leading to more complete ablations. A 2-year follow-up revealed that the 106 patients in a randomized study (the Simplicity HTN-2 trial) had a mean reduction in office systolic and diastolic blood pressure of 32/12 mmHg at 6 months [5]. However, only a small subgroup's worth of data from ambulatory blood pressure monitoring were available, and the results were

based on office blood pressure. The data revealed a less dramatic drop in blood pressure (11/7 mmHg in 24-hour blood pressure) after six months [9]. Whether the BP drop continued during the long-term follow-up is also unknown [6]. Only patients with more severe RH, whose ambulatory blood pressure remains uncontrolled even after four or more antihypertensive medications—including those that block mineralocorticoid receptors—will be considered for the renal sympathetic denervation procedure. Renal denervation not only lowers blood pressure but also enhances glucose metabolism, helps patients with congestive heart failure regain their functional status, and has a positive effect on end organ damage such as LVH, arterial stiffness, and albuminuria.

5.2.2 Baroreflex Activation Therapy

Baroreflex activation therapy is an implantable device that lowers blood pressure by decreasing the sympathetic response by electrically stimulating carotid sinus baroreceptors. The Rheos pivotal trial involved patients with hypertension and was a double-blind, randomized, placebo-controlled device trial [7]. After, the average office systolic blood pressure dropped by as much as 35 mmHg. After a year, more than half of the participants had their systolic blood pressure under control. This effect continued over a longer follow-up period of 22–53 months. Remarkably, ambulatory blood pressures were not assessed in this trial; office blood pressure reduction was the sole outcome. Ambulatory blood pressure was measured in a related European trial known as DEBUT—Device Based Therapy. After a year, there was an average reduction of 30 mmHg in office systolic blood pressure and an average reduction of 13 mmHg in ambulatory systolic blood pressure. As a result, there are still some unsolved issues and uncertainty surrounding this procedure's future. To ascertain the long-term safety and whether adding new medications will lower ambulatory blood pressure, more research is required.

5.2.3 The Carotid Body Ablation

Caused by carotid body ablation Increased carotid body sensitivity was observed in hypertension patients, according to research using both human subjects and animal models; the reason for this abnormality is unknown. In a small, randomized, crossover, placebo-controlled study, the deactivation of CB chemoreceptors by hyperoxia (respiration with 100% oxygen) attenuated the enhanced muscle sympathetic nerve activity in untreated hypertensive men [9]. The controls showed no signs of change. Furthermore, it has been shown that, in hypertensive patients, hyperoxia momentarily lowers blood pressure, but not in controls with normal blood pressure. These results imply that the development of sympathetic overactivity in hypertension may be pathogenetically related to tonic chemoreceptor drive [1]. Surgery to remove the carotid bodies has been performed on humans to treat ailments other than hypertension, like bronchial asthma and COPD. A patient with hypertension saws a reduction in blood pressure from 170 to 130 mmHg after five days of carotid body removal and six months of bilateral carotid body surgery; a patient with normotension did not see any change in blood pressure. Although the first human studies on the effects of unilateral or bilateral carotid body resection for hypertension have not yet been finished, they are currently underway.

5.2.4 Arteriovenous Fistula

The self-expanding device creates a 4 mm AVF between the vein and iliac artery in just one hour, resulting in an 800 ml/minute sustained calibrated shunt volume. There are several mechanisms that are thought to cause BP to decrease after AVF formation. Even with an increase in cardiac output, the main mechanism is a decrease in total systemic vascular resistance. Improved tissue oxygen delivery from higher arterial oxygen content may reduce renal and peripheral chemoreceptor activation, which in turn may reduce sympathetic activity. A decrease in effective arterial volume and systemic vascular compliance may also enhance arterial compliance and lessen the workload on the heart, even in the presence of elevated cardiac output. In the first randomized controlled trial of this method, ambulatory blood pressure monitoring confirmed a 27 mmHg decrease in office systolic blood pressure in the six-month intervention group, compared with a 4 mmHg fall in the normal care group. Not used because venous stenosis and thrombosis induction, as well as the development of right heart failure, are anticipated side effects Generally.

5.2.5 Renal artery stent placement

It is controversial to employ stents in percutaneous transluminal angioplasty for renal artery stenosis. Renal artery bypass grafts provide little to no benefit when used to control blood pressure, maintain kidney function, prevent cardiovascular disease, or prevent renal events, according to recent clinical trials. Stent placement for renal artery stenosis in hypertensive patients [12]. Fibromuscular lesion angioplasty is recommended as a treatment option for hypertension because it is nearly always advantageous and frequently resolves associated hypertension. Endovascular angioplasty with or without stenting should be considered when medication therapy fails and there is poorly controlled hypertension with a cardiovascular risk. Because of the high rate of procedure-related adverse events, renal artery revascularization was not used frequently in the ASTRAL trial, which prevented a clinically meaningful reduction in blood pressure.

6.CONCLUSION

Use lifestyle modifications in addition to blood pressure-lowering medications for the secondary prevention of recurrent cardiovascular events in adults with clinical CVD (CHD, CHF, and stroke) and an average systolic blood pressure of 130 mmHg or an average diastolic blood pressure of 80 mmHg.

An average of five different antihypertensive medications is not enough to lower a patient with TRH's SBP below 160 mmHg when they receive interventional blood pressure lowering therapy. Two interventional strategies—renal denervation and baroreflex activation therapy—are used in clinical practice more often than other strategies, like artery stenting and AVF. Blood pressure should be less than 130/80 mmHg in patients with diabetes mellitus, CHF, CKD, after renal transplantation, and to prevent secondary stroke in lacunar stroke. ACE inhibitors, ARBs, or thiazide diuretics are the first drugs to be prescribed. In three to four weeks, follow-up blood pressure and electrolyte assessments are performed. It might be essential to take more medication or raise the dosage. Frequent visits are recommended during dose adjustment; each visit should include an assessment of medication adherence and lifestyle factors, in addition to at-home blood pressure monitoring. We recommend monitoring every six months after the blood pressure falls to less than 130/80 mmHg.

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