# Restoring Vascular Homeostasis: Integrating Functional Nutrition into the Hypertensive Clinical Paradigm

## I. INTRODUCTION

Hypertension, commonly known as high blood pressure, is a medical condition defined by consistently elevated pressure in the arteries. The disease burden of hypertension is said to be associated with growing life expectancy and lifestyle. The condition affects 30-40% of adults globally (1). It is rightly called “the silent killer” because it is asymptomatic in nature and may go undetected for a long time. It is the major modifiable concomitant risk factor for cardiovascular disease (CVD) and premature death, accounting for about 45% of CVD morbidity and mortality in the world (2).

Hypertension can be categorized into two different forms: (a) Primary hypertension (b) Secondary hypertension. Primary or essential hypertension is diagnosed when blood pressure is persistently at or above 140/90 mm Hg without any known secondary etiology (3). Unhealthy dietary habits and a sedentary lifestyle are generally important and potentially reversible environmental factors that contribute to elevated blood pressure. Approximately 10% of the cases are characterized as secondary hypertension, associated with a particular remediable underlying cause. In case the cause is correctly diagnosed and treated, patients suffering from secondary hypertension can successfully have an improvement in blood pressure control and even achieve a normalized blood pressure in addition to CVD risk reduction (4). Historically, even in children, the most common form of hypertension was secondary; however, recent trends exhibit a major shift. It is currently primary hypertension that is a significant cause of elevated blood pressure in children above six years of age. According to a multicenter study, 43% of children with high blood pressure were diagnosed with primary hypertension. Moreover, essential hypertension was the dominant underlying cause of hypertension in children above 6 years of age (3).

According to the International Society of Hypertension (ISH), hypertension can be classified into 4 categories based on blood pressure readings (5):

- **Normal:** Systolic less than 130 and Diastolic less than 85 mm Hg
- **High-Normal:** Systolic 130 to 139 and Diastolic between 85-89 mm Hg
- **Grade 1 hypertension:** Systolic 140 to 159 or Diastolic 90 to 99 mm Hg
- **Grade 2 hypertension:** Systolic greater than or equal to 160 mm Hg or Diastolic greater than or equal to 100 mm Hg

Besides these classifications, two more clinical phenomena are also included under the same guidelines:

- **White Coat Hypertension:** It is an office blood pressure between 130/80 mm Hg and 160/100 mm Hg, but stabilizes to 130/80 mm Hg or lower after a minimum of three months of anti-hypertensive therapy. Ambulatory or home blood pressure measurement is generally required for it to be diagnosed.
- **Masked Hypertension:** It is characterized by high office blood pressure with systolic between 120-129 mm Hg and diastolic less than 80 mm Hg, but increased blood pressure on ambulatory or home measurements, that is 130/80 mm Hg or higher.

Hypertension is a burning health concern that is increasing substantially on a global scale, particularly in low-income and middle-income countries. According to the World Health Organization (WHO) Global Report 2023, about 1.3 billion adults were living with hypertension by the year 2019. Additionally, only 54% of adults with high blood pressure are diagnosed, 42% are on treatment and 21% have stable blood pressure. Analyzing the trend of the condition regionally, it was found that there is a stark contrast between European and Asian countries. In 2019, the WHO European Region witnessed a decrease in the percentage of hypertensive adults as compared to 1990, whereas the Asian region saw a significant increase during the same period. The prevalence of hypertension particularly increased in the Western Pacific Region, which includes China, Vietnam, Malaysia, Japan, the Philippines, the Republic of Korea, New Zealand, and Australia, from 24% to 28%. It is even more concerning that the number of adults with hypertension in this region more than doubled from 144 million in the year 1990 to 346 million in 2019. Furthermore, the WHO Southeast Asia Region, encompassing countries like Indonesia, Thailand, India, and Nepal, saw the prevalence rates rise from 29% to 32% (6). In India, an estimation of 220 million people suffering from hypertension, only 12% of them have successfully managed to bring their blood pressure under control (7). Over the past three decades, from 1999 to 2019, the number of hypertensive adults in the WHO European region and the WHO region of the Americas increased by 41%. On the other hand, a substantial increase of 144% was observed in the WHO South-East Asia and the WHO Western Pacific region (8). Thus, it has now become an urgent need to emphasize controlling hypertension, especially in these regions in order to alleviate the onset of CVDs.

## II. PATHOPHYSIOLOGY OF HYPERTENSION

Many pathophysiological conditions drive the development and persistence of hypertension. Some of these factors contributing to its prevalence include:

### A. Alterations in the Renin-Angiotensin-Aldosterone System (RAAS)

The Renin-Angiotensin-Aldosterone System (RAAS) is a critical regulator of blood pressure regulation, blood volume and water homeostasis. In the pathophysiological condition of hypertension, RAAS often becomes dysregulated, leading to its overactivation.

#### (i) Increase in Vasoconstriction

The process initiates with the release of renin from the kidneys, which leads to the production of Angiotensin II. Angiotensin II is one of the potent vasoconstrictors known; it binds to Angiotensin II Type 1 Receptor (AT1-R) on the plasma membrane of vascular smooth muscle cells, thereby causing contraction of smooth muscles that constrict the blood vessels, leading to an increase in systemic vascular resistance (9).

#### (ii) Sodium and Water Retention

The RAAS regulates blood pressure and volume through aldosterone. The adrenal cortex releases aldosterone, stimulated by angiotensin II. Aldosterone acts on the distal convoluted tubules and collecting ducts of the kidneys to increase sodium and water reabsorption, thereby resulting in water retention. This further leads to an expansion in plasma volume, raising the pressure against arterial walls (9). Recent studies have revealed that the RAAS, particularly Angiotensin II through AT1-R activation in the kidney's proximal tubules, is vital in maintaining basal blood pressure and contributing to Angiotensin II-induced hypertension by regulating sodium reabsorption in the proximal tubule and the pressure-natriuresis response (10).

#### (iii) Structural Vascular Remodeling

Angiotensin II can also act like a growth factor, promoting hypertrophy of vascular smooth muscle cells and increasing deposition of collagen. This leads to structural vascular remodeling, making the arteries thicker and stiffer, and also contributes to the pathophysiology of hypertension. This structural remodeling is a major phenomenon that maintains elevated blood pressure in hypertensive adults, essentially "fixing" the condition, reducing its response to temporary physiological fluctuations, and aiding in the persistence of the illness (11).

### B. Sympathetic Nervous System (SNS) Hyperactivity

The SNS is studied to play a key role in regulating blood pressure. In hypertensive adults, the SNS is mostly defined by chronic overactivity, which triggers several neurogenic pathways, thereby keeping blood pressure consistently elevated (12).

#### (i) Neurogenic Vasoconstriction

The SNS manages to keep the vascular tone in control by releasing norepinephrine which binds to α-adrenergic receptors present in the smooth muscle of peripheral arterioles. Consequently, activation of these receptors results in vasoconstriction, reducing blood vessel diameter and increasing peripheral resistance- factors responsible for driving high blood pressure in early or "neurogenic" hypertension.

#### (ii) Rise in Cardiac Output

The SNS also impacts the heart in a direct manner, in addition to its effect on blood vessels. Both the catecholamines (norepinephrine and epinephrine) trigger β-adrenergic receptors in the heart that result in an increase in heart rate and the force of heart contractions. The combined effect of these factors together enhances the total cardiac output, further contributing to the hypertensive condition.

#### (iii) SNS and the Kidneys

The SNS has a critical role to play in renal function, with increased sympathetic activity in the renal nerves triggering the release of renin. This results in the activation of the RAAS producing angiotensin II, which further enhances vasoconstriction and release of aldosterone. Additionally, SNS activation also promotes the reabsorption of sodium as well as water in the renal tubules and reduces renal blood flow along with glomerular filtration rate (GFR), creating a self-reinforcing loop of volume expansion and vasoconstriction.

### C. Endothelial Dysfunction and Nitric Oxide (NO) Deficiency

The endothelium, a single layer of cells that lines the entire vascular system, serves as a major organ for maintaining vascular homeostasis, and regulating certain aspects like vascular tone, permeability, inflammation, and blood coagulation. In a healthy state, the endothelium synthesizes vasoactive substances that keep a balance between vasodilation through nitric oxide, prostacyclin, and endothelium-derived hyperpolarizing factors, and vasoconstriction, generally favouring vasodilation to ensure optimal blood circulation. However, the endothelial lining is often compromised in hypertensive population that leads to a state of chronic constriction and inflammation (13).

#### (i) Reduction of Nitric Oxide (NO) Bioavailability

Nitric Oxide (NO) serves as a potent vasodilator for a healthy cardiovascular system. Produced by healthy endothelial cells, NO ensures that the blood vessels remain relaxed. Any impairment in its production or even breakdown by reactive oxygen species (ROS) is a defining characteristic of endothelial dysfunction and a major contributor to the development of hypertension. The reduction in NO synthesis or its absence prevents blood vessels from proper dilation that leads to increased vascular stiffness and constriction causing an elevation in blood pressure.

#### (ii) Oxidative Stress and Inflammation

The accumulation of ROS generates a state of oxidative stress that leads to the damage of the endothelial lining. The damage to the lining stimulates an inflammatory reaction that attracts white blood cells in circulation, pulling them into the vessel wall and releasing pro-inflammatory cytokines like IL-6. This inflammatory environment causes aging and stiffness in the arteries and leaves the vascular system impaired.

#### (iii) Increase in Endothelin-1 Production

Oversynthesis of endothelin-1 by dysfunctional endothelial cells results in chronic vasoconstriction and reduced NO availability. The lack of balance in this condition tips the vascular system towards vasoconstriction, peripheral resistance, inflammation, and structural vascular remodeling. The transition from vasodilation to consistent vasoconstriction are the key drivers behind atherosclerosis, arterial stiffness, and hypertension.

### D. Genetics and Epigenetics

Hypertension is a multifactorial health condition with a significant hereditary influence, with genetics believed to contribute to 30% to 70% of the variation in blood pressure levels (14). However, primary hypertension does not stem from a single gene; instead, it arises from the complex interplay between a number of genetic variants as well as environmental factors.

**(i) Polygenic Risk and Sodium Handling**

The majority of the cases of primary hypertension are considered "polygenic," referring to the point that they arise from the cumulative effect of several minor genetic variants known as Single Nucleotide Polymorphisms, or SNPs. A significant number of these variants are found in or near genes that regulate blood pressure either by sodium handling by the kidneys or the contraction of vascular smooth muscles or the RAAS. While the presence of any single variant may not lead to an elevation in blood pressure, however, carrying multiple risk alleles can significantly diminish an individual's threshold for developing the condition.

**(ii) Rare Monogenic Forms**

Unlike the prevalent polygenic variant, specific rare forms of hypertension result from mutations in a single gene (monogenic) that lead to serious and early-onset of high blood pressure. These typically affect the RAAS pathways and are usually a result of mutations that lead to an increase in sodium reabsorption, volume expansion, and a decrease in renin production, as well as salt-sensitive hypertension (15). Changes in the mechanisms regulating the epithelial sodium channel (ENaC) within the kidneys, such as in Liddle Syndrome is an example of monogenic hypertension. These offer valuable understanding of the underlying disease mechanisms as they illustrate how a solitary flaw in sodium transport can result in severe hypertension that begins early in life.

**(iii) Epigenetic Modifications**

Epigenetics refers to modifications in gene expression that occur without changes to the DNA sequence itself. Factors including dietary habits, stress levels, and aging can trigger DNA methylation or histone alteration, which can either activate or deactivate specific genes involved in regulating blood pressure. This provides insight into why individuals with identical genetic structures may exhibit varying blood pressure levels influenced by their personal experiences and surroundings. A few important epigenetic mechanisms involved in blood pressure regulation are DNA methylation, modification of histone proteins, and miRNA downregulation.

| Category | Primary Mechanism | Physiological Impact | Long-term Consequence |
|---|---|---|---|
| **RAAS Dysregulation** | Overproduction of Angiotensin II | Potent vasoconstriction; stimulates Aldosterone for sodium ion and water retention | Structural Remodeling: Permanent thickening and stiffening of arterial walls |
| **SNS Hyperactivity** | Chronic Norepinephrine release | Increases heart rate (cardiac output) and triggers neurogenic vasoconstriction | Self-Reinforcing Loop: Triggers further Renin release, worsening volume expansion |
| **Endothelial Dysfunction** | Reduced Nitric Oxide (NO) bioavailability | Impaired vasodilation; shift toward a pro-inflammatory, constricted state | Atherosclerosis: Increased oxidative stress (ROS) leading to arterial aging and stiffness |
| **Vascular Tone** | Endothelin-1 Oversynthesis | Shifts balance from vasodilation to chronic vasoconstriction | Increased peripheral resistance and systemic vascular damage |
| **Genetic Factors** | Polygenic (SNPs) vs. Monogenic (e.g., Liddle Syndrome) | Altered renal sodium handling and epithelial sodium channel (ENaC) function | Increased hereditary susceptibility and early-onset hypertension |

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| **Epigenetics** | DNA Methylation & Histone alteration | Environmental factors (stress, diet) "turn on/off" blood pressure genes | Variable BP levels in individuals with similar genetic backgrounds |

**Table 1:** Pathophysiological conditions of hypertension with its long term consequences

## III. ROOT CAUSES ASSOCIATED WITH HYPERTENSION

### A. Mineral Imbalances and Nutrient Deficiencies

**(i) Magnesium Deficiency:** The sodium-potassium pump is regulated by magnesium. Its deficiency allows for salt and calcium to build up inside the cells, which directly stimulates vascular constriction and hypertension.

**(ii) Potassium Deficiency:** The body uses and eliminates sodium efficiently when it has enough potassium. It becomes extremely sensitive to sodium when potassium levels are low, which raises blood pressure.

**(iii) Calcium Deficiency:** Inadequate calcium intake triggers secondary activation of the parathyroid gland, which moves calcium from bones into the blood and smooth muscle tissues, increasing blood pressure.

**(iv) Soft Drinking Water:** Populations consuming "soft water" (water stripped of its natural calcium and magnesium) have significantly higher rates of cardiovascular disease and hypertension.

### B. Dietary Toxins and Excesses

**(i) Refined Sugar and Fructose:** High sugar consumption drives insulin resistance. Furthermore, the breakdown of high-fructose corn syrup produces uric acid, which directly increases blood pressure by inactivating nitric oxide (a crucial molecule that normally relaxes and dilates blood vessels). Sugar also causes Advanced Glycation End products (AGEs) that damage blood vessels.

**(ii) Processed Sodium/Salt:** While the "salt hypothesis" is highly debated for healthy individuals, excessive intake of processed, inorganic sodium chloride—especially when not balanced by potassium—dehydrates cells, strains the kidneys, and increases blood volume pressure.

**(iii) Alcohol and Caffeine:** Regular consumption of alcohol damages internal organs and is cited as a leading cause of high blood pressure. Caffeine acts as a sympathetic nervous system stimulant that constricts blood vessels.

**(iv) Industrial Seed Oils:** Consumption of unnatural fats (like trans fat and highly processed vegetable oils) promotes oxidative stress and inflammation, damaging the endothelial lining of the arteries.

### C. Metabolic and Endocrine Disorders

**(i) Insulin Resistance:** A key component of metabolic syndrome, insulin resistance is the main underlying cause of essential hypertension. It elevates blood pressure by causing compensatory hyperinsulinemia, which triggers kidney sodium retention, increases sympathetic nervous system activity, impairs nitric oxide-mediated vasodilation, and promotes vascular remodeling.

**(ii) Obesity:** Obesity causes insulin resistance, overactivates the sympathetic nervous system, activates the RAAS, and physically compresses the kidneys, increasing sodium retention and driving high blood pressure.

## IV. MANAGEMENT OF HYPERTENSION

The management of hypertension has progressed to a highly effective strategy that aims to lower systemic vascular resistance and blood volume to avert damage to vital organs. Current clinical guidelines stress the importance of beginning with lifestyle modifications like dietary changes, physical exercise, weight management, etc., followed by targeted classes of medication. Two approaches are usually followed to manage hypertension, one of which is conventional or pharmacological treatment (16), and the other is functional nutrition-based or non-pharmacological treatment.

### A. Conventional Intervention

For individuals living with severe hypertension, medications are conventionally preferred. These medications are categorized into:

- **First-Line Pharmacological Treatments**

**(i)Thiazide-type diuretics:** These medications, including chlorthalidone and indapamide, lower blood pressure by aiding the kidneys to expel excess salt and water, which reduces both blood volume and cardiac output.

**(ii) Calcium Channel Blockers (CCBs):** CCBs, for example amlodipine, obstruct calcium channels in the smooth muscle of arteries, resulting in vasodilation and a decrease in systemic vascular resistance.

**(iii) Angiotensin-Converting Enzyme (ACE) inhibitors:** ACE inhibitors, such as benazepril, inhibit the formation of angiotensin II from angiotensin I. Angiotensin II is a vasoconstrictor that triggers secretion of aldosterone, thus lowering systemic vascular resistance and blood pressure. The ACE inhibitors possess renoprotective effects, benefitting patients suffering from chronic kidney disease.

**(iv) Angiotensin II Receptor Blockers (ARBs):** ARBs, such as valsartan, selectively inhibit the AT1-R for angiotensin II, resulting in reductions in blood pressure comparable to ACE inhibitors but generally with a reduced occurrence of cough. Similar to ACE inhibitors, they provide benefits for people with chronic kidney disease.

- **Secondary and Other Specialized Medications**

**(i) Beta-blockers:** Beta-blockers including metoprolol and carvedilol are now typically not advised as standard first-line treatments unless certain specific comorbidities are present, such as post-myocardial infarction, heart failure with reduced ejection fraction, or atrial fibrillation that requires rate control.

**(ii) Alpha-blockers:** Alpha-blockers like doxazosin, are second-line medications used to manage essential hypertension.

**(iii) Central-acting agents:** These agents, including clonidine, are used for resistant hypertension.

**(iv) Direct Vasodilators:** These are employed in complex or resistant hypertensive cases.

**(v) Mineralocorticoid receptor antagonists:** These are basically aldosterone antagonists that block aldosterone, reducing sodium/water retention and blood pressure. Spironolactone is the preferred fourth-line medication for resistant hypertension.

**(vi) Combination Therapy and Treatment:** Numerous patients might require multiple medications to reach their blood pressure targets. Early combination therapy is often suggested for patients with grade 2 hypertension, especially if they are at a higher risk for cardiovascular issues. Commonly recommended dual combinations typically involve an ACEI/ARB paired with a CCB or an ACEI/ARB paired with a thiazide diuretic. Combining medications that function through different mechanisms can result in enhanced effects and better blood pressure regulation, all while with minimum side effects.

| Category | Drug Class | Examples | Mechanism of Action | Clinical Notes & Indications |
|---|---|---|---|---|
| **First-Line** | Thiazide-type Diuretics | Chlorthalidone, Indapamide | Promotes renal elimination of sodium ion and water; reduces blood volume and cardiac output. | Effective for volume-dependent hypertension. |

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| **First-Line** | Calcium Channel Blockers (CCBs) | Amlodipine | Inhibits calcium ion influx in arterial smooth muscle, leading to vasodilation. | Decreases systemic vascular resistance (SVR). |
| **First-Line** | ACE Inhibitors | Benazepril | Blocks conversion of Angiotensin I to Angiotensin II; inhibits aldosterone. | Renoprotective; preferred for Chronic Kidney Disease (CKD). |
| **First-Line** | Angiotensin II Receptor Blockers (ARBs) | Valsartan | Selectively blocks AT1 receptors. | Similar to ACE inhibitors but with lower incidence of cough |
| **Secondary** | Beta-blockers | Metoprolol, Carvedilol | Reduces heart rate and contractility. | Used for specific comorbidities (Post-MI, Heart Failure, Atrial Fibrillation) |
| **Secondary** | Alpha-blocker | Doxazosin | Blocks α-adrenergic receptors on vascular smooth muscle | Used for essential hypertension; second-line choice |

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| **Specialized** | Central-acting Agents | Clonidine | Stimulates α2-adrenergic receptors in the brain to reduce sympathetic outflow | Reserved for resistant hypertension |
| **Specialized** | Direct Vasodilators | Hydralazine | Directly relaxes vascular smooth muscle | Used in complex or refractory cases |
| **Specialized** | Mineralocorticoid Receptor Antagonists | Spironolactone | Blocks aldosterone; reduces sodium/water retention | Fourth-line medication specifically for resistant hypertension |

**Table 2:** Different categories of medications under conventional management of hypertension

### B. Functional Nutrition-Based Intervention

Functional nutrition offers an advanced approach that goes beyond basic dietary needs. It emphasizes specific food components and functional foods to achieve certain health goals. For managing hypertension, this strategy takes advantage of the complex relationships among nutrients, bioactive substances, and bodily processes. These connections can influence blood pressure through various ways, including regulating blood vessel tone, reducing oxidative stress, managing inflammation, and improving endothelial function. Fundamental to this pathophysiology is the disturbance of regular vascular balance, which can be recognized and tracked using particular blood biomarkers.

- **Key Blood Markers associated with Hypertension**

**(i) Inflammatory Biomarkers**

**High Sensitivity C-Reactive Protein (hs-CRP):** It is an important protein secreted by the liver, which serves as an important marker for low-grade vascular inflammation and the stratification of cardiovascular risk. As a highly sensitive test, it is able to measure low levels of CRP in plasma, which is important for the assessment of cardiovascular risk.

**Erythrocyte Sedimentation Rate (ESR):** ESR is an important biomarker of inflammation, which measures the rate at which red blood cells (erythrocytes) settle to the bottom of a standardized vertical tube. This phenomenon of falling is referred to as "sedimentation." RBCs normally fall faster in patients with inflammatory diseases like infections, malignancies, and autoimmune diseases. These conditions result in an increase in the concentration of proteins in the blood. The high protein concentration leads to an increased tendency of RBCs to clump and fall faster.

**Interleukin-6 (IL-6):** This pro-inflammatory cytokine is vital in the inflammatory process and is independently correlated with the risk of hypertension, contributing to increased vascular resistance

**Tumor Necrosis Factor-alpha (TNF-α):** TNF-α fosters vascular inflammation and disrupts endothelial function, with heightened levels noted in individuals with hypertension, especially among those experiencing complications.

**(ii) Oxidative Stress Markers**

**Homocysteine:** Elevated homocysteine is a strong indicator and cause of oxidative stress, which results in vascular, neurological, and tissue injuries. High concentration of homocysteine stimulates the production of ROS, which decreases the activity of antioxidant enzymes and causes endothelial dysfunction.

**Selenium:** Selenium is an important biomarker for oxidative stress, which is associated with endothelial dysfunction and hypertension. Low selenium levels result in reduced activity of selenium-dependent enzymes, particularly glutathione peroxidase, being directly related to high levels of oxidative damage and ROS production.

**Uric Acid:** High serum uric acid level is a key marker and mediator of oxidative stress in hypertension, indicating enhanced xanthine oxidase activity rather than being a mere antioxidant. Elevated uric acid concentration causes endothelial dysfunction and vascular smooth muscle cell proliferation, which directly contribute to the development of hypertension. Although uric acid is a natural antioxidant, in the hypertensive environment, it acts as a pro-oxidant associated with an increase in the production of ROS.

**(iii) Vascular Dysfunction Markers**

**Lipoprotein(a) [Lp(a)]:** It is a genetically driven, established risk factor with pro-inflammatory and pro-thrombotic properties. Because of its homology with plasminogen, Lp(a) inhibits the body's physiological mechanisms of clot lysis, thereby substantially raising the risk of acute vascular events and damage to the arterial wall. Elevated [Lp(a)] concentrations are known as a "dual threat" risk factor for cardiovascular disease, especially in hypertensive patients. This risk factor is operative through pro-atherogenic and pro-thrombotic pathways, in addition to the mechanical effects of hypertension, thereby raising the risk of acute cardiovascular events such as myocardial infarction and stroke.

**Apolipoprotein B (ApoB):** ApoB is the key protein component of all potentially atherogenic lipoprotein particles, such as VLDL, and LDL, with one molecule per particle. In hypertensive patients, a high ApoB count suggests a likelihood that these particles will be pushed into the subendothelial space due to high hydrostatic pressure. This will trigger the formation of atherosclerotic plaques, converting functional hypertension into structural vascular disease.

- **Evidence-Based Dietary Patterns for Hypertension Management**

**(i) DASH Diet**

The Dietary Approaches to Stop Hypertension (DASH) diet is one of the most studied nutritional methods for managing blood pressure. Recent reviews and meta-analyses continue to show its effectiveness in lowering both systolic and diastolic blood pressure in different populations. The DASH diet focuses on fruits, vegetables, whole grains, lean proteins, and low-fat dairy products while limiting sodium, saturated fats, and added sugars.

As per a study conducted, the DASH diet decreases systolic blood pressure by an average of 6.74 mmHg and diastolic blood pressure by 3.54 mmHg as compared to control diets (17). These results were similar across various demographic groups and stages of hypertension, showing the diet's wide-ranging benefits. The reasons for these benefits include higher intake of potassium, magnesium, calcium, and fiber, along with lower sodium and saturated fat consumption.

**(ii) Mediterranean Diet**

The Mediterranean diet is characterized by a high intake of olive oil, fruit, vegetables, legumes and whole grains and moderate consumption of fish and wine. This is an excellent diet to help manage hypertension. Recent research has found that it's especially good at reducing systolic blood pressure when people also restrict their sodium consumption. A study found the Mediterranean diet to be more effective than both the DASH diet and salt reduction alone, for lowering office systolic blood pressure. Both dietary patterns worked better than salt restriction alone. However, there were no significant differences in diastolic or 24-hour ambulatory blood pressure outcomes between the dietary interventions (18). The benefits of the Mediterranean diet come from its high levels of monounsaturated fatty acids, polyphenols, antioxidants, and anti-inflammatory compounds.

- **Key Nutritional Components and Their Mechanisms**

**(i) Sodium and Potassium Balance**

The sodium-potassium balance is very important for controlling blood pressure with food. Most people focus on cutting down on sodium. New research shows that consuming more of potassium can also help. A review in 2023 by Sriperumbuduri *et. al* described that one should focus on both sodium and potassium intake. They noted that increasing potassium intake can lower blood pressure effectively and offer additional cardiovascular benefits. The mechanisms behind this include better sodium excretion, reduced blood vessel resistance, and RAAS modulation (19).

**(ii) Magnesium and Calcium**

Magnesium deficiency is recognized as a common factor in the development of hypertension. Recent studies have highlighted a number of ways magnesium affects blood pressure regulation. These include its influence on sympathetic tone, vascular tone, kidney potassium management, aldosterone release, and inflammation pathways. Similarly, calcium is also crucial for functioning of vascular smooth muscle and blood pressure management. Evidence suggests that getting enough calcium helps control blood pressure, especially when paired with other mineral treatments.

**(iii) Dietary Fiber and Protein**

Dietary fiber intake has been linked to lowering blood pressure. This is likely due to better insulin sensitivity, decreased inflammation, and modulation of gut microbiota. Recent meta-analyses show that fiber supplements can noticeably reduce both systolic and diastolic blood pressure, especially in people with hypertension. Protein intake, especially from plant sources, is also important for controlling blood pressure. A 2023 review found that higher protein intake, particularly from quality plant sources, effectively helps manage blood pressure. However, the review pointed out that protein deficiency in some groups complicates nutritional solutions, requiring focused strategies (20).

- **Functional Foods and Nutraceuticals**

**(i) Probiotics and Gut Microbiome Modulation**

The gut microbiome plays an important role in regulating blood pressure. Hence, probiotics and prebiotics are promising potential treatments for hypertension management. Recent research indicates that an imbalance in gut microbiota can lead to hypertension. This occurs through several factors, including changes in short-chain fatty acid production, increased gut permeability, and effects on the gut-brain axis. Chen *et al*. in their study discussed probiotics as functional food ingredients that may help lower hypertension. They work by regulating oxidative stress, improving endothelial function, and reducing inflammation (21). A combination of probiotics and prebiotics could therefore be a new approach for managing hypertension by targeting the intestinal flora. However, more studies are necessary to refine these formulations and confirm their long-term effectiveness.

**(ii) Polyphenols and Antioxidant Compounds**

Dietary polyphenols, especially flavonoids, have shown significant effects in lowering blood pressure through various mechanisms. Dietary polyphenols help protect against high blood pressure through antioxidant action, reducing inflammation, inhibiting ACE, and remodeling blood vessels. The gut microbiota’s ability to absorb and break down polyphenols is vital for their therapeutic effects. Flavan-3-ols, a type of polyphenol found in cocoa and green tea, have shown promising improvement in endothelial function and lowering blood pressure.

**(iii) Bioactive Peptides and Other Nutraceuticals**

Food-derived bioactive peptides have received a lot of attention as nutraceuticals for managing hypertension, mainly because of their ACE inhibitory activity. Ichim *et al.* discussed the potential of bioactive peptides from foods in treating hypertension. However, it is to be noted that more human clinical trials are being encouraged to explore their full potential (22). A few other promising nutraceuticals include lycopene, carotenoids, and various plant-based compounds. Carotenoids have promising therapeutic potential for managing hypertension due to their antioxidant, anti-inflammatory, and endothelial-improving properties (23). Likewise, lycopene and a few other carotenoids have demonstrated effectiveness in both preclinical and clinical studies, however, comprehensive human trials are needed to confirm their therapeutic benefits.

**(iv) Omega-3 Rich Foods**

Foods that have a high content of omega-3 fatty acids, especially fatty fish, walnuts, and flaxseeds, are important for managing blood pressure through several mechanisms. These essential fatty acids become part of cell membranes, improving membrane flexibility and receptor function. Omega-3 fatty acids also have strong anti-inflammatory effects. They reduce the production of pro-inflammatory eicosanoids, which can harm blood vessels. The benefits of omega-3 fatty acids in lowering blood pressure are especially notable for those with stage II hypertension. Clinical studies show that they can lower systolic blood pressure by 3-6 mmHg. Besides lowering blood pressure, foods high in omega-3 also improve endothelial function, reduce arterial stiffness, and enhance heart rate variability. All these factors contribute to better cardiovascular health.

**(v) Garlic (*Allium sativum*)**

Garlic exerts a strong natural vasodilatory effect mainly due to the release of hydrogen sulfide and the stimulation of nitric oxide synthase. The active compound allicin in garlic competitively inhibits the action of Angiotensin II, a hormone that causes vasoconstriction, thus replicating the action of the drug ACE inhibitors. Clinical trials have indicated that the regular intake of garlic can result in a substantial reduction in both systolic and diastolic blood pressure due to the improvement in arterial distensibility and a reduction in peripheral resistance.

**(vi) Green Tea (*Camellia sinensis*)**

Green tea exerts a blood pressure-lowering effect mainly due to its high content of epigallocatechin gallate (EGCG) and other polyphenolic catechins. These compounds are potent antioxidants that counteract the action of reactive oxygen species, which are harmful to the vascular endothelium. By protecting the inner lining of the blood vessels, green tea increases the availability of nitric oxide, which is the body’s major vasodilatory signal. In addition, the regular intake of green tea has been linked to a reduction in arterial stiffness, which is a characteristic of chronic hypertension.

**(vii) Coconut Water**

Coconut water acts as a functional drink because of its high potassium content, which is a major electrolyte in regulating blood pressure. Potassium helps in the elimination of excess sodium in the body by the kidneys and also relieves tension in the walls of blood vessels. The regulation of the sodium-potassium ratio achieved by coconut water helps in the normalization of the volume of intravascular fluids and also relieves the mechanical tension in the walls of arteries.

| Category | Component/Biomarker | Primary Mechanism of Action | Clinical Significance |
|---|---|---|---|
| **Inflammatory Markers** | hs-CRP, ESR, IL-6, TNF-α | Systemic inflammation drives endothelial dysfunction and vascular resistance | High levels indicate structural vascular damage and high risk for complications |
| **Vascular Dysfunction** | [Lp (a)], ApoB | Quantifies particle burden and pro-thrombotic risk | Identifies the density of potential plaque infiltrating pressure-damaged vessels |
| **Dietary Patterns** | DASH & Mediterranean | High K+, Mg2+, and polyphenols; low Na+ and saturated fats | DASH: Lowers SBP by 6.7 mmHg and DBP by 3.5 mmHg<br><br>Mediterranean: Superior for SBP when sodium is restricted |
| **Minerals** | Sodium-Potassium Balance | Potassium promotes Na+ elimination and modulates the RAAS | High K+ intake lowers SVR and provides cardiovascular protection |

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| **Micronutrients** | Magnesium & Calcium | Regulates vascular smooth muscle tone and sympathetic nervous activity | Deficiency is a common driver of essential hypertension |
| **Nutraceuticals** | Bioactive Peptides | Acts as a natural ACE inhibitor | Derived from food sources; potential for pharmacological-like effects |
| **Bioactives** | Polyphenols & Flavonoids | Antioxidant action; inhibits ACE and protects endothelial cells | Found in cocoa, green tea; highly dependent on gut microbiome health |
| **Lipids** | Omega-3 Fatty Acids | Improves membrane flexibility; reduces pro-inflammatory eicosanoids | Lowers SBP by 3–6 mmHg in Stage II patients; improves heart rate variability |
| **Gut Health** | Probiotics & Prebiotics | Modulates short-chain fatty acids (SCFAs); reduces gut permeability | Targets the gut-brain axis to reduce neurogenic hypertension |
| **Lifestyle** | Regular exercise, stress management, and proper sleep | Regular exercise improves blood pressure; Stress management and proper sleep decrease cortisol levels | Controls SNS hyperactivity |

**Table 3:** Functional Nutrition and Biomarker-Driven Interventions for Hypertension Management

- **Implementation Strategies and Clinical Considerations**

**(i) Personalized Nutrition Approaches**

The emerging field of personalized nutrition presents great potential for improving hypertension management with dietary interventions. Recent progress in understanding individual differences in nutrient metabolism, genetic factors, and microbiome composition has led to more targeted nutritional strategies. The effective use of functional nutrition methods requires taking individual factors into account, such as age, gender, ethnicity, health conditions, and personal preferences. Personalized approaches can enhance adherence and results, although more research is necessary to create standardized guidelines for tailored nutritional interventions in hypertension management (24).

**(ii) Integration with Conventional Therapy**

Functional nutrition approaches should work alongside conventional medication instead of being seen as replacements. Recent evidence shows that nutritional interventions can improve medication effectiveness, lower required dosages, and possibly reduce side effects. While diets like DASH, and Mediterranean along with certain nutraceuticals, have shown significant potential in lowering blood pressure, they cannot completely replace blood pressure medications when needed. They serve as complementary treatments, particularly in cases of moderate to severe hypertension.

**(iii) Addressing Implementation Barriers**

Despite strong evidence for functional nutrition approaches, several barriers limit their use in clinical practice. These include challenges with patient adherence, socioeconomic factors, cultural preferences, and the lack of training for healthcare providers in nutrition counseling. Certain issues like adherence, socioeconomic factors, and cultural preferences restrict the implementation of dietary interventions. This makes it necessary to develop tailored approaches to improve their practical use in clinical settings. Creation of nutritional strategies that are culturally sensitive, economically feasible, and personally acceptable is important to boost implementation success and achieve long-term, sustainable improvements in our health.

- **Future Directions and Research Gaps**

**(i) Emerging Therapeutic Targets**

Ongoing research is focused on discovering new therapeutic targets for nutritional interventions aimed at managing hypertension. These targets encompass specific molecular pathways, the composition of gut microbiota, and genetic variations that affect individual responses to dietary changes. Recent investigations have pointed out the potential benefits of targeting particular gut microbial species and their metabolites to regulate blood pressure. Additionally, new findings indicate that dietary components may induce epigenetic changes that significantly contribute to the prevention and treatment of hypertension, although more research is necessary to fully understand these processes.

### (ii) Technological Innovations

Innovations in technology, such as mobile health applications, artificial intelligence, and personalized monitoring devices, present new possibilities for both implementing and tracking nutritional interventions in the management of hypertension. It was highlighted in a review that utilizing technologies like mHealth is crucial for enhancing the comprehensiveness and sustainability of hypertension treatment (25).

### (iii) Research Priorities

A number of key research areas have come to light for enhancing functional nutrition strategies in the management of hypertension. These areas encompass extensive, long-term clinical studies; determination of the best nutrient combinations and dosages; and creation of standardized protocols to integrate nutritional interventions with traditional therapies. Future research should aim to tackle existing challenges, such as discrepancies in study designs, a lack of uniformity in outcome measures, and a limited understanding of the long-term effects and safety profiles associated with various nutritional interventions. Moreover, additional studies are required to explore the interactions among different nutritional elements and their collective impacts on blood pressure regulation.

## V. CONCLUSION

Hypertension stands as one of the most significant global health issues today, impacting millions around the globe and serving as a major factor in cardiovascular-related illnesses and fatalities. Although conventional medication strategies have been the mainstay of treatment for many years, there is increasing awareness that a nutrition-focused approach can yield better results for the long-term management of blood pressure. This shift from conventional medication to functional nutrition acknowledges that hypertension is more than just a numerical irregularity; it is a multifaceted metabolic condition linked to inflammatory processes, oxidative stress, endothelial dysfunction, and inadequate nutrition. Approaches based on functional nutrition provide a promising, evidence-backed method for managing hypertension, yielding benefits that go beyond merely lowering blood pressure to include better cardiovascular health, improved quality of life, and diminished healthcare expenses.

Even scientific research strongly endorses the incorporation of well-structured nutritional strategies into comprehensive protocols for hypertension management. Dietary patterns such as the DASH diet, Mediterranean diet, and plant-based approaches have shown consistent effectiveness in lowering blood pressure among various populations. Certain nutrients and functional foods—such as minerals, omega 3-rich foods, garlic, polyphenols, probiotics, and bioactive peptides—present targeted therapeutic possibilities through a variety of physiological mechanisms. Although considerable advancements have been achieved in comprehending the mechanisms and effectiveness of dietary interventions, additional study is required to fine-tune protocols, tackle implementation challenges, and confirm long-term safety and efficacy. In addition, functional nutrition works best when combined with lifestyle changes. Regular exercise improves the blood pressure-lowering effects of diet changes by boosting blood vessel function, reducing inflammation, and improving insulin sensitivity. Stress management techniques, such as meditation, yoga, and getting enough sleep, support nutritional efforts by lowering activity in the sympathetic nervous system and decreasing cortisol levels, both of which can lead to high blood pressure. The blend of functional nutrition and these lifestyle changes creates benefits that are greater than just adding up each individual approach. Effective implementation necessitates tailored strategies, awareness of personal and cultural influences, and incorporation with standard therapy.

The future of managing hypertension is likely to be found in integrated strategies that merge the strengths of traditional medicine with research-backed nutritional interventions, customized to suit individual preferences and requirements. As research progresses in enhancing our understanding of the links between nutrition and blood pressure, functional nutrition strategies are set to take on a more significant role in global efforts for hypertension prevention and treatment.

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