

New advances in the treatment and diagnosis of hypertension in primary care: a literature review

Novos avanços no tratamento e diagnóstico da hipertensão na atenção primária: uma revisão de literatura

Nuevos avances en el tratamiento y diagnóstico de la hipertensión en atención primaria: una revisión de la literatura

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This article contributes to the debate on the diagnosis and treatment of hypertension in primary care, a disease that is on the rise globally and that needs theoretical and epistemically discussion to assist policies to confront the disease.

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The article reviews the cutting-edge literature and provides a synthesis with a proposed research agenda for new studies.

ABSTRACT

Background: Despite the availability of safe and effective antihypertensive drugs, hypertension continues to be a major risk factor for cardiovascular death and morbidity worldwide. This review explores the contemporary landscape of advances in hypertension (HTN) diagnosis and treatment, examining the discordant diagnostic thresholds proposed by American and European guidelines. **Methods:** An integrative approach was employed, analyzing pertinent literature from sources such as ScienceDirect, Google Scholar, and PubMed. Inclusion criteria encompassed studies on new advances in HTN diagnosis and treatment in primary care, published in English within the last five years (2018-2023). **Results:** Diagnostic innovations focus on the preference for automated sphygmomanometers and technological advancements, enhancing precision and reliability. Treatment advancements span neurovascular dimensions, including neuromodulation, and innovations in the renin-angiotensin-aldosterone system, showcasing promising drugs like *finerenone* and *esaxerenone*. Sodium-glucose cotransporter-2 inhibitors demonstrate efficacy beyond antidiabetic effects. The complexities of renal denervation and its challenges are scrutinized, emphasizing the need for further research. Clinical decision-making underscores risk stratification, lifestyle modifications, and the emerging use of single-pill combinations and individualized treatment plans. **Conclusion:** The review highlights the multidimensional approach required for optimal HTN management in primary care, encompassing diagnostic innovations, treatment advancements, and individualized strategies. Ongoing research is pivotal for refining diagnostic and therapeutic paradigms in hypertension management.

Keywords: Hypertension in primary care, diagnosis, treatment, recent advances.

RESUMO

Antecedentes: Apesar da disponibilidade de medicamentos anti-hipertensivos seguros e eficazes, a hipertensão continua a ser um importante fator de risco para morte e morbidade cardiovascular em todo o mundo. Esta revisão explora o panorama contemporâneo dos avanços no diagnóstico e tratamento da hipertensão (HA), examinando os limiares diagnósticos discordantes propostos pelas diretrizes americanas e europeias. **Métodos:** Foi empregada uma abordagem integrativa, analisando literatura pertinente de fontes como ScienceDirect, Google Scholar e PubMed. Os critérios de inclusão abrangeram estudos sobre novos avanços no diagnóstico e tratamento da hipertensão na atenção primária, publicados em inglês nos últimos cinco anos (2018-2023). **Resultados:** As inovações diagnósticas concentram-se na preferência por esfigmomanômetros automatizados e nos avanços tecnológicos, aumentando a precisão e a confiabilidade. Os avanços no tratamento abrangem dimensões neurovasculares, incluindo neuromodulação e inovações no sistema renina-angiotensina-aldosterona, apresentando medicamentos promissores como a finerenona e a esaxerenona. Os inibidores do cotransportador-2 de sódio-glicose demonstram eficácia além dos efeitos antidiabéticos. As complexidades da denervação renal e seus desafios são examinados, enfatizando a necessidade de mais pesquisas. A tomada de decisão clínica sublinha a estratificação de risco, as modificações no estilo de vida e o uso emergente de combinações de comprimidos únicos e planos de tratamento individualizados. **Conclusão:** A revisão destaca a abordagem multidimensional necessária para o manejo ideal da hipertensão na atenção primária, abrangendo inovações diagnósticas, avanços no tratamento e estratégias individualizadas. A pesquisa em andamento é fundamental para refinar os paradigmas diagnósticos e terapêuticos no tratamento da hipertensão.

Palavras-chave: Hipertensão na atenção primária, diagnóstico, tratamento, avanços recentes.

RESUMEN

Antecedentes: A pesar de la disponibilidad de fármacos antihipertensivos seguros y eficaces, la hipertensión sigue siendo un importante factor de riesgo de muerte y morbilidad cardiovascular en todo el mundo. Esta revisión explora el panorama contemporáneo de los avances en el diagnóstico y tratamiento de la hipertensión (HTA), examinando los umbrales de diagnóstico discordantes propuestos por las guías estadounidenses y europeas. **Métodos:** Se empleó un enfoque integrador, analizando la literatura pertinente de fuentes como ScienceDirect, Google Scholar y PubMed. Los criterios de inclusión abarcaron estudios sobre nuevos avances en el diagnóstico y tratamiento de la HTA en atención primaria, publicados en inglés en los últimos cinco años (2018-2023). **Resultados:** Las innovaciones diagnósticas se centran en la preferencia por esfigmomanómetros automatizados y avances tecnológicos, que mejoran la precisión y la confiabilidad. Los avances en el tratamiento abarcan dimensiones neurovasculares, incluida la neuromodulación, y las innovaciones en el sistema renina-angiotensina-aldosterona, mostrando fármacos prometedores como la finerenona y la esaxerenona. Los inhibidores del cotransportador 2 de sodio-glucosa demuestran eficacia más allá de los efectos antidiabéticos. Se analizan las complejidades de la denervación renal y sus desafíos, enfatizando la necesidad de realizar más investigaciones. La toma de decisiones clínicas subraya la estratificación del riesgo, las modificaciones del estilo de vida y el uso emergente de combinaciones de una sola pastilla y planes de tratamiento individualizados. **Conclusión:** La revisión destaca el enfoque multidimensional necesario para el manejo óptimo de la HTA en atención primaria, que abarca innovaciones en el diagnóstico, avances en el tratamiento y estrategias individualizadas. La investigación en curso es fundamental para perfeccionar los paradigmas diagnósticos y terapéuticos en el tratamiento de la hipertensión.

Palabras clave: Hipertensión en atención primaria, diagnóstico, tratamiento, avances recientes.

INTRODUCTION

Different nations in the Atlantic have different ideas about what HTN is nowadays. The 2018 European Society of Cardiology/European Society of Hypertension (ESC/ESH) guidelines maintain the traditional threshold of office BP levels above 140/90 mmHg for the definition of hypertension, whereas the 2017 American College of Cardiology/American Heart Association (ACC/AHA) guidelines set the threshold at 130/80 mmHg⁴ (Williams et al. 2018) (Whelton et al. 2018).

Notably, the US guidelines' more stringent diagnostic objectives do not imply that pharmacological therapy is necessary for every person whose office blood pressure falls between 130 and 139/80 and 89 mmHg. The AHA/ACC recommendations advise against using medication therapy for these patients and instead recommend using more suitable lifestyle strategies (weight management, quitting smoking, adopting a low-sodium diet, etc.) (Whelton et al. 2018).

Notably, all guidelines concur that medication therapy should begin right away for the following patients: (a) those with office blood pressure of at least 160/100 mmHg, regardless of other factors;(Verdecchia, Reboldi, and Angeli 2020) (b) those with blood pressure of at least 140/90 mmHg who also have heart failure, cerebrovascular disease, or ischemic heart disease (Verdecchia, Reboldi, and Angeli 2020).

Hypertension continues to be a major risk factor for cardiovascular disease and mortality due to its high prevalence and significant clinical effect (Mills et al. 2016). According to Verdecchia, Cavallini, and Angeli over 1.5 billion persons globally had office blood pressure (BP) measurements in 2015 that were more than 140 mmHg systolic or 90 mmHg diastolic (Verdecchia, Cavallini, and Angeli 2022). In 1990, 331 million women and 317 million men were diagnosed with hypertension; by 2019, however, the number of individuals aged 30-79 years who had a previous diagnosis has doubled to 626 million women and 652 million men, despite a steady age-standardized prevalence globally (Zhou et al. 2021). A systolic blood pressure of at least 140 mmHg is thought to account for over 70% of the global burden of illness and death (Forouzanfar et al. 2017).

The percentage of treated hypertensive patients with normal blood pressure, or "controlled hypertension," is still very low globally despite such remarkable increase. According to estimates, this percentage is close to 23% for women and 18% for male (Zhou et al. 2021). Notably, there are still significant differences in hypertension diagnosis, treatment, and management around the globe, even if they have improved in the majority of industrialized and high-income nations. In reality, almost two thirds of hypertension sufferers reside in low-income nations (Mills, Stefanescu, and He 2020). Several nations in sub-Saharan Africa and Oceania have not seen gains in hypertension knowledge, treatment, or management during the last 20 years (Angeli, Reboldi, and Verdecchia 2012)(Angeli, Reboldi, and Verdecchia 2013).

First and foremost, it should be noted that although arterial hypertension is becoming more commonplace and has a greater clinical effect globally, its management is still inadequate, especially in low-income nations. A second point to examine is that, in the last several years, there has been an astounding lack of novel investigations, despite the enormous amount of observational studies and randomized controlled trials that have been done during the previous forty years. Dzau observed in a thorough analysis that there is a sharp halt to research on novel antihypertensive medications and therapeutic targets (Dzau and Balatbat 2019). Furthermore, according to Dzau and Balatbat, there hasn't been any current effort to create therapeutic applications based on the several genetic variants linked to hypertension. It should be remembered that a novel antihypertensive medication may take more than ten years from its original invention to its commercialization, and that this might result in a final cost of more than two billion US dollars. Within this framework, the majority of industry efforts are focused on maximizing the use of established and efficacious antihypertensive medications (e.g., new combinations, new dosages, etc.) and redirecting these toward hypertension via the use of blood pressure-lowering medications that were originally developed for other diseases (e.g., gliflozines, drugs for heart failure, etc.) (Hunter, Chapman, and Dhaun 2021).

The review article's objective is to thoroughly analyze current advances in the primary care setting's diagnosis and treatment of hypertension. The main objective is to provide light on new developments and perspectives in the clinical treatment of hypertension, offering insightful information that will help patients getting primary care achieve better cardiovascular outcomes and blood pressure control rates.

METHODS

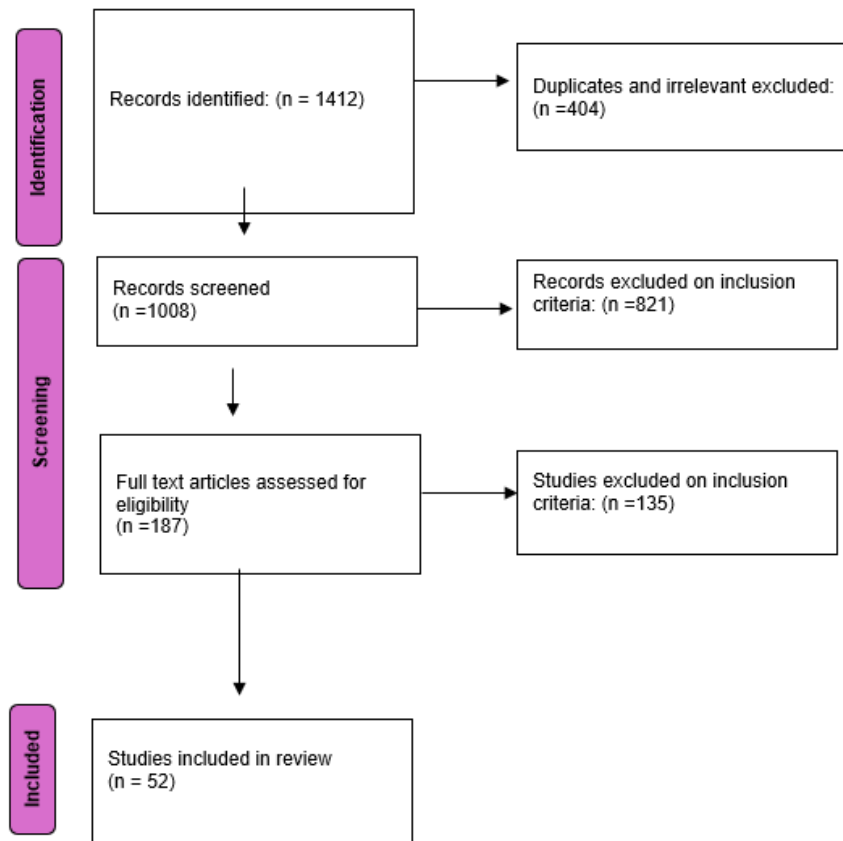
This review adopts an integrative approach, systematically examining and evaluating relevant material sourced from scholarly databases such as ScienceDirect, Google Scholar, and PubMed. Search terms such as "hypertension," "diagnosis," "treatment," and "primary care" were employed to search the literature. Boolean operators (AND, OR) were utilized for refining search queries and focusing on pertinent literature.

Inclusion and Exclusion Criteria:

Studies emphasizing new advances in the diagnosis and treatment of hypertension in primary care, published in English within the last five years (2018-23), are eligible for inclusion. Research involving non-human subjects, irrelevant outcomes, or substandard methodologies were excluded. A preliminary screening using abstracts and titles as primary criteria resulted in the identification of 1412 articles. Application of inclusion and exclusion criteria narrowed down the selection to 187 articles. A comprehensive review involved a full-text examination, ultimately including 52 articles that contribute valuable evidence to this review.

A systematic approach was employed to categorize literature review results on recent advances in the diagnosis and treatment of hypertension in primary care. Analytical categories were established for clarity and consistency, focusing on innovative approaches and technologies. Diagnostic advancements included ambulatory blood pressure monitoring, wearable devices, and artificial intelligence applications in hypertension diagnosis. Treatment breakthroughs were categorized into pharmacological interventions, lifestyle modifications, and treatment strategies using AI. This systematic categorization facilitates a comprehensive understanding of the diverse advancements in hypertension diagnosis and treatment within the primary care setting.

Figure 1. Flowchart with the stages of the literature review



Source: own elaboration (2023)

RESULTS AND DISCUSSION

Diagnosing and measuring blood pressure

One of the biological indicators that is assessed the most often and influences decisions in a variety of clinical contexts is blood pressure (BP). The most precise method is still direct measurement using intra-arterial catheters, but it is only suitable for intraprocedural monitoring or very sick patients because to its invasive nature. For most applications, indirect measurement with automated sphygmomanometers is the recommended approach. Such certified devices are increasingly being used for both stationary and ambulatory measures because to their growing accuracy and dependability. Arrhythmias reduce their accuracy, but cutting-edge technologies aim for even greater precision (Kitt et al. 2019). Conversely, the manual

method is continuously falling short due to its considerable intra- and inter-observer variability.

Ambulatory blood pressure monitoring, or ABPM, is essential in identifying patients with concealed or white-coat hypertension, providing details on sleep-dipping status, and improving the identification of people who are really resistant to hypertension. Compared to office stationery blood pressure checks, they form a more reliable predictor of HTN-mediated organ damage when combined with home blood pressure monitoring (HBPM) (Leontsinis et al. 2020). Unfortunately, since data for out-of-office measurements is unavailable, the treatment objectives that are currently available are based on office BP readings¹.

There is ongoing debate concerning the appropriate conditions for obtaining office blood pressure measurements. Several studies support the theory that the unattended approach, in which no health professional is present throughout the operation, attenuates the white-coat phenomenon, resulting in results that are lower than those of the standard attended method (Andreadis et al. 2019). According to available research, there is a strong correlation between both methods and organ damage caused by HTN (Salveti et al. 2019). Furthermore, there seems to be no correlation between the approach used and the positive outcome of intensive therapy in SPRINT (Johnson et al. 2018). Given the need for a uniform approach, the measurement technique's methodology is essential.

The commercialization of electronic devices intended for remote blood pressure (BP) monitoring and transmission is being propelled by the growing ubiquity of digital health technologies. Although these devices have the potential to improve population-level blood pressure management and the diagnosis of hypertension, their validation and reliability remain a concern (Hunter, Chapman, and Dhaun 2021). Notably, there are concerns about the limits of various BP measuring equipment on the market, and not all of them follow the current criteria. Cuff-less continuous blood pressure monitoring devices are becoming more popular, yet research is still needed to determine their validity and reliability. Easy wearability, accuracy validation, connection to secure digital archives, accessibility for medical practitioners, and identification of important blood pressure parameters for prognosis and organ damage prediction are crucial elements in guaranteeing the dependability of such systems (Parati et al. 2014). The incorporation of artificial intelligence into the datasets produced by these systems might provide insightful information on how to effectively manage hypertension.

New advances in treatment:

Neurovascular dimension in hypertension: neuromodulation

Though not entirely understood, the sympathetic nervous system plays a role in both cardiovascular homeostasis and dysfunction. Pharmacological or interventional methods that attempt to downregulate or restore the sympathetic outflow transmission at various levels are referred to as neuromodulation.

Previously, to lessen the sympathetic overdrive in HTN, the pharmaceutical sector focused on a number of loci. Due to their lack of selectivity for peripheral tissues, these attempts include the use of centrally acting medications, such as adrenergic blockers, which have varying degrees of success and serious adverse effects. Another strategy is highlighted by recent laboratory and preclinical outcomes. In animal experiments, the alpha-1D adrenergic receptor vaccine ADRQ β -004 showed strong antihypertensive effect (Li et al. 2019). A neurosteroid drug called allopregnanolone was also discovered to lower blood pressure by selectively altering gamma-aminobutyric acid-a receptors (Head, Jackson, and Gueguen 2019).

It is essential to understand how inflammation and autonomic dysfunction interact. Vascular aging, arterial stiffness, and elevated blood pressure have all been closely linked to endothelial dysfunction. An essential component of this mechanism is angiotensin II (Piqueras and Sanz 2020). Beyond the blood-brain barrier (BBB), recent research links inflammation to a baroreflex imbalance. According to some theories, hypertensive individuals may have compromised blood-brain barrier integrity, which may lead to autonomic dysfunction (Setiadi et al. 2018). Several factors have been suggested as mediators of neuroinflammation, including oxidative stress, inflammatory cytokines, renin-angiotensin system (RAS) hyperactivation, and astrocyte dysfunction. These factors then modify the activity of several central nerve cardioregulatory units, leading to HTN⁴⁴. Novel compounds have the ability to modulate inflammation in the nervous system. By lowering cerebral angiotensin III and vasopressin release, firibastat has been shown to reduce blood pressure (Llorens-Cortes and Touyz 2020). Because of its ability to prevent microglia activation, minocycline is being studied for resistant HTN.

The second primary pillar of neuromodulation, device-based therapies, is a rapidly developing area in the treatment of HTN. Many various approaches to potentially stop or control the sympathetic impact on target organs and the systemic vasculature have been attempted (Tsioufis, Schmieder, and Mancia 2016).

The interventional approach that has been studied the most is catheter-mediated renal denervation (RDN). In the therapy of HTN, carotid baroreceptor stimulation and arteriovenous fistula creation have also been explored; these approaches will not be covered in this review. Subjects with resistant HTN showed substantial decreases in blood pressure in early RDN investigations that used radiofrequency ablation. The SIMPLICITY HTN-3 trial was discouraging, but new data from second-generation sham-controlled studies unquestionably show that RDN is safe and has positive short-term effects on

blood pressure control in individuals with mild, moderate, or resistant HTN (Stavropoulos et al. 2020). This puts RDN back in the spotlight. Patients with end-stage renal illness showed comparable effectiveness in a smaller cohort (Scalise et al. 2020). Numerous factors are responsible for the above indicated favorable outcomes. These include expanding operator expertise, learning more about the architecture of the renal arteries, designing better studies, and implementing innovative catheters that allow ablation at many locations (Lauder et al. 2018). Remarkably, results from a number of trials have extended RDN's use beyond the management of hypertension. Despite not using the sham control approach, ERADICATE-AF researchers corroborated the fact that RDN with atrial fibrillation ablation led to better results (Steinberg et al. 2020).

Renin angiotensin aldosterone system

Finerenone showed a lower incidence of hyperkalemia in the ARTS-DN study, although its effectiveness as an antihypertensive was limited (Stewart, Lavie, and Ventura 2018). In a phase III RCT (ESAX-HTN), esaxerenone recently outperformed eplerenone in terms of hypertensive effectiveness and safety (Ito et al. 2018).

Aldosterone synthase is inhibited by aldosterone synthase inhibitors (CYP11B2), which lowers the amounts of circulating renin and aldosterone. The first-in-class medication LCI699 was withdrawn because it was shown to concurrently inhibit CYP11B1, which increased adrenocorticotrophic hormone in response. The creation of agents that are more selective is the main goal of current efforts (Hoyt et al. 2017).

Recently, it was shown that there is another RAAS route that causes vasodilatation and natriuresis. It is mediated by the angiotensin-converting enzyme (ACE) 2's conversion of angiotensin II to angiotensin (1,7). Potential targets for new antihypertensive medicines include ACE2 activators, angiotensin (1,7) agonists, and angiotensin receptor 2 (AT2) agonists. However, these medications have not shown positive outcomes so far. In the NEW-HOPE trial, centrally acting aminopeptidase A inhibitor firibastat decreased blood pressure levels (Ferdinand, Harrison, and Johnson 2020).

Antagonists of Endothelin Receptors

The original purpose of ET-1 receptor antagonists (ERAs) was to treat pulmonary arterial hypertension (PAH). There have always been aspirations for them to grow in HTN. A recent meta-analysis of 18 trials including 4,898 hypertensive patients found that, at the expense of more severe side effects, there was a substantial decrease in office and 24-hour ABP monitoring associated with ERAs (Yuan et al. 2017).

Due to its ability to inhibit both endothelin-A and endothelin-B receptors and its extended pharmacological half-life (about 44 hours), apakintan has been shown to be more effective than lisinopril and placebo (Verweij et al. 2020). As per Trenszt et al. (2019), this antihypertensive agent appears to exert additional mechanisms beyond the expected positive effects of sustained BP-lowering action, such as a decrease in renal vascular resistance and left ventricular hypertrophy. This finding lends credence to the theory that the new agent could expand our antihypertensive toolkit in resistant hypertension (Trenszt et al. 2019).. Administering apakintan to patients with resistant hypertension is now the focus of the PRECISION phase III trial 5.4.

Dual-action inhibitors of RAS and neprilysin

A metalloprotease called neprilysin (NEP) is in charge of breaking down brain natriuretic peptide and atrial natriuretic peptide (Ito et al. 2018). Concomitant degenerative effects on vasoconstrictive peptides, including endothelin and angiotensin II, hindered efforts to produce an antihypertensive NEP inhibitor. As a result, studies on two different routes that combined NEP and RAS inhibition continued. The development of omapatrilat, a dual NEP-ACE inhibitor, was halted due to safety concerns about angioedema, despite its notable ability to decrease blood pressure. Researchers developed LCZ696 because angiotensin receptor blockers (ARBs) have a lower chance of causing angioedema. Recently, valsartan and sacubitril combined to form a dual AT2-NEP inhibitor (ARNI) was approved as a therapy for heart failure with decreased ejection fraction (HFrEF). Its effectiveness in lowering blood pressure has been shown in several studies (Solomon et al. 2019). Additionally, ARNIs are more effective against HTN compared with ARBs alone while exhibiting comparable safety, according to a meta-analysis of 11 RCTs (Malik and Aronow 2022).

Inhibitors of the sodium-glucose cotransporter-2

These are new oral hypoglycemic medications that prevent glucose from being renally reabsorption in the proximal tubule (Briassoulis, Al Dhaybi, and Bakris 2018). The three approved sodium-glucose cotransporter-2 inhibitors (SGLT2is), dapagliflozin, canagliflozin, and empagliflozin, all showed impressive class-effect outcomes regarding hospitalizations for heart failure, progression of diabetic nephropathy, and cardiovascular and all-cause mortality. These studies marked a turning point in the development of cardioprotective and nephroprotective anti-diabetic drugs (Kluger et al. 2019).

Selective SGLT2 receptor inhibitors, such as empagliflozin, canagliflozin, dapagliflozin, and ertugliflozin, somewhat decreased systolic and diastolic blood pressure in pivotal phase III clinical studies (Malik and Aronow 2022). These processes may include natriuresis, osmotic diuresis, and decreased sympathetic tone. The risk of heart failure was significantly reduced

by these medications (Malik and Aronow 2022). Empagliflozin and dapagliflozin decreased cardiovascular mortality and the requirement for re-hospitalizations for heart failure in patients with heart failure and reduced ejection fraction (HFrEF), both with and without diabetes (Takaki et al. 2000). Empagliflozin reduced the risk of cardiovascular mortality or heart failure hospitalization by 21% in individuals with heart failure with preserved ejection fraction (HFpEF) (De Vecchis, Ariano, and Soreca 2018).

In addition to providing glycemic management and having a positive cardiorenal effect, all relevant studies showing SGLT2is showed a little but considerable reduction in blood pressure levels (Sanidas et al. 2020). But as recent meta-analyses have shown, there is only a modest drop in blood pressure (Baker et al. 2017). Major concerns have been expressed about possible side effects because to the increased frequency of fractures, diabetic ketoacidosis, urinary tract infections, and limb amputations seen in some of the leading SGLT-2 (Steiner 2016).

Denervation of the Renal System

Hypertension is a condition that is influenced by the overactivity of the renal sympathetic nervous system. The basis for renal denervation's entrance into clinical practice was established by its shown ability to lower blood pressure and enhance renal function in animal models of hypertension (DiBona and Esler 2010).

Many expectations about the therapeutic efficacy of renal denervation were raised by several clinical studies that were published in the last 15 years (Fengler et al. 2019). Regretfully, in terms of the efficacy of decreasing blood pressure, the SIMPLICITY HTN-3 studies were unable to prove that renal denervation was better than sham control (Bhatt et al. 2014). The SIMPLICITY HTN-3 studies did, however, have a number of methodological issues. The study included patients with secondary hypertension (hyperaldosteronism, etc.), 34% of operators had only performed one denervation procedure previously, drug treatment was significantly more intense in the "sham" control group than in the denervation group, and in 75% of cases, denervation was not "complete" (not all renal artery quadrants were ablated). These are just a few of the limitations of the study. As a consequence, the problem was reexamined in its entirety, and additional, better-designed clinical studies were planned and carried out, with encouraging findings (Azizi et al. 2018).

Eighty patients with resistant hypertension were randomized in the SPYRAL HTN-ON MED study to receive medication therapy either with or without radiofrequency renal denervation (mock operation). At six months following the treatment, the average 24-hour systolic blood pressure decreased by 9.0 mmHg with renal denervation and only by 1.6 mmHg with the sham procedure ($p < 0.05$) (Azizi et al. 2018). In the SPYRAL HTN-OFF MED Pivotal study, 331 patients who were not receiving treatment were randomly assigned to have radiofrequency renal denervation or a sham surgery. Three months after the treatment, the average 24-hour systolic blood pressure decreased by 4.7 mmHg following renal denervation and by 0.6 mmHg following the sham procedure ($p < 0.05$) (Böhm et al. 2020). Overall, in terms of BP decrease after 3 to 6 months, these additional studies decisively showed the advantages of renal denervation over the sham surgery.

Clinical decision-making: managing hypertension

In the current period, cardiovascular illness is a well-known socioeconomic burden. Despite notable advancements in prevention, rates of morbidity, death, and disability linked to major cardiovascular events are still quite high (Forouzanfar et al. 2017). Risk stratification strategies have garnered substantial investment from health systems worldwide (Whelton et al. 2018). They concentrate on primary as well as secondary prevention. In the first, asymptomatic people are referred to, and the goal is to identify early subclinical manifestations of the illness or those who are more susceptible to developing a cardiovascular condition. It is becoming harder and harder to prevent HTN. This work is very difficult because to factors including obesity, sedentary lifestyles, poor diets, excessive salt consumption, smoking, and associated morbid illnesses like diabetes and obstructive sleep apnea, as well as an aging population (Leontsinis et al. 2020). The second pertains to individuals who have been diagnosed with cardiovascular disease and focuses on modifying risk factors and implementing other organized treatments aimed at enhancing life expectancy and quality of life.

First-line course of care

As per the most recent guidelines, the primary therapeutic intervention for hypertension still involves a significant shift in lifestyle, with an emphasis on consistent physical activity, incorporating a healthier diet, losing weight, limiting the intake of salt, caffeine, and alcohol, and quitting smoking. Most intriguingly, these actions may potentially take the place of medication therapy in individuals with grade 1 HTN, since they seem to postpone the onset of the condition. Moreover, they lower the risk of cardiovascular disease and improve the efficacy of medication treatment plans (Visseren et al. 2021).

Treatment with a single tablet combination: the new strategy

The most recent ESC/ESH recommendations advise starting with a single pill combination (SPC) of two medications from each of the five main classes and, if necessary, titrating up to a three-drug SPC. Patients with grade 1 HTN and low/moderate risk, fragile elderly patients (especially if systolic blood pressure is less than 150 mmHg), and people with high-

normal blood pressure are the exceptions who should be given first consideration for monotherapy.¹ The 2017 ACC/AHA recommendations recommend a two-drug combination for patients with stage 2 HTN with an average blood pressure greater than 20/10 mmHg over their target blood pressure, whereas a single medication is recommended for individuals with stage 1 HTN (Whelton et al. 2018). Because they target diverse processes, drug combinations are both more efficacious and more tolerated than maximum dosage monotherapies. The SPC regimen improved rates of blood pressure management and medication adherence, and as a result, improved cardiovascular outcomes are anticipated (Schoonhoven et al. 2018).

Hard-to-control and resistant hypertension

Managing difficult-to-control hypertension (HTN) is still an important clinical practice issue, even with advances in HTN treatment, a wide range of drug classes with powerful combinations, and even with the increasing use of selective serine proteases (SPCs). This is because patients with difficult-to-control hypertension are more vulnerable to HTN-mediated organ damage, chronic kidney disease and cardiovascular events. To meet the criteria for resistant hypertension, a minimum of three drugs must be taken at optimal or well-tolerated dosages, including diuretics. To rule out the typical pseudo-resistance situations, failure to meet the BP goal should be verified by ABPM or HBPM, and treatment compliance should be considered (Leontsinis et al. 2020). Obesity, excessive alcohol and salt consumption, prescription and over-the-counter medications that cause hypertension, undetected secondary hypertension, and severe HTN-mediated organ damage such as chronic kidney disease and large-artery stiffness are other major causes of hard-to-control hypertension. Following a thorough evaluation, it is predicted that less than 10% of treated individuals have real resistant HTN prevalence (Krieger et al. 2018).

Towards advances in the diagnosis and treatment of hypertension in primary care: discussion of the results

The American and European guidelines' differing diagnostic criteria for hypertension (HTN) highlight the continuing controversy in the medical profession (Whelton et al., 2018). The European recommendations maintain the conventional cutoff of 140/90 mmHg, but the American guidelines support a stricter threshold of 130/80 mmHg (Williams et al., 2018). Interestingly, the American recommendations emphasize lifestyle changes over pharmaceutical intervention for patients lying between the two thresholds; this is despite the fact that the diagnostic thresholds differ (Whelton et al., 2018). This study sheds light on the changing landscape of hypertension management by examining recent developments in the diagnosis and treatment of hypertension in primary care.

The measurement of blood pressure (BP) is still essential for diagnosing hypertension. Although direct intra-arterial catheter measurements are precise, their wide-spread adoption is limited by their invasive nature. Due to their growing accuracy and dependability, automated sphygmomanometers are becoming to be the standard option for both ambulatory and stationary blood pressure monitoring. Technological innovations are meant to improve accuracy, especially when arrhythmias are present (Kitt et al., 2019). On the other hand, considerable intra- and inter-observer variability is present in manual procedures, underscoring the need for more dependable diagnostic techniques.

The review emphasizes neuromodulation as a possible treatment option while examining different aspects of the neurovascular side of hypertension. According to recent research, neurosteroid medications and vaccinations targeting the alpha-1D adrenergic receptor may have promising results (Li et al., 2019; Head, Jackson, and Gueguen, 2019). Furthermore, hypertension individuals may benefit from developments in the renin-angiotensin-aldosterone system, such as the introduction of finerenone and esaxerenone (Stewart, Lavie, and Ventura, 2018; Ito et al., 2018). Effective techniques to treat hypertension are shown by investigating endothelin receptor antagonists, dual-action inhibitors of the renin-angiotensin system, and neprilysin (Yuan et al., 2017). In addition to being effective as antidiabetic medications, sodium-glucose cotransporter-2 inhibitors also provide remarkable results in heart failure and cardiovascular mortality (Briasoulis, Al Dhaybi, and Bakris, 2018; Kluger et al., 2019).

The conversation also includes renal denervation, which, in spite of early fervor, has trouble establishing superiority over sham control in clinical trials (Bhatt et al., 2014). The complexity of the study design, which includes patient selection and procedural completeness, adds to the uncertainty about the effectiveness of the research. These results emphasize the need for further investigation and a more comprehensive comprehension of hypertension therapies.

The use of risk stratification measures is crucial in mitigating the socioeconomic impact of cardiovascular disease. Although there have been significant breakthroughs in primary and secondary preventive techniques, the identification of high-risk patients and subclinical symptoms still remains the key emphasis (Forouzanfar et al., 2017). According to research, lifestyle changes may sometimes postpone or even take the place of pharmaceutical therapy, which is why they are still the primary line of treatment (Visseren et al., 2021).

A novel approach to managing hypertension is the use of single-pill combinations (SPCs), which are intended to increase drug adherence and improve cardiovascular outcomes (Schoonhoven et al., 2018). The need of customized treatment programs is emphasized, taking into account variables including age, risk, and blood pressure levels. Chronically difficult-to-manage and resistant hypertension necessitates a thorough assessment of the underlying causes and the

exploration of alternative therapeutic modalities (Leontsinis et al., 2020; Krieger et al., 2018).

CONCLUSIONS AND FINAL REMARKS

In conclusion, this review synthesizes recent literature on hypertension, encompassing diagnostic innovations, treatment advancements, and strategies for clinical decision-making. The evolving landscape of hypertension management calls for a multidimensional approach, integrating lifestyle modifications, novel therapeutics, and individualized treatment plans to achieve optimal outcomes in primary care settings. Ongoing research and clinical trials will play a pivotal role in shaping the future of hypertension management, emphasizing the need for continuous exploration and refinement of diagnostic and therapeutic strategies.

There are inherent limits to this thorough evaluation of the literature on recent developments in the diagnosis and management of hypertension in primary care. First off, the inclusion criteria were limited to English-language articles published during the last five years, which could have excluded older but still relevant research or applicable non-English studies. Furthermore, the study may have a selection bias since it did not include all of the literature that was accessible on the subject due to its dependence on databases like ScienceDirect, Google Scholar, and PubMed. Furthermore, the variety of evidence taken into consideration may be reduced if studies with poor methodology are excluded. Moreover, the study focuses on advances related to hypertension in primary care settings, which may mean that some developments relevant to intermediate or tertiary care settings are missed.

More research is necessary to improve our grasp of the most current developments in the treatment of hypertension. Future research should examine the relative efficacy of various diagnostic technologies, including wearables, artificial intelligence apps, and ambulatory blood pressure monitoring. A side-by-side comparison of various technologies might clarify their unique advantages and disadvantages, helping medical professionals make the best decision depending on the needs of their patients. The analysis also highlights the need of doing research on novel medications and therapeutic targets. Research has slowed down recently; future studies should concentrate on closing this gap and advancing preclinical findings into clinical applications. A more comprehensive strategy to managing hypertension may be offered by investigating the viability and efficacy of integrating many cutting-edge therapeutic modalities, such as renin-angiotensin-aldosterone system inhibitors and neurovascular modulation.

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B. data research and statistical analysis:	20%	20%	20%	20%	20%
C. elaboration of figures and tables:	20%	20%	20%	20%	20%
D. drafting, reviewing and writing of the text:	20%	20%	20%	20%	20%
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