Dietary Intervention to Improve Blood Pressure Control: Beyond Salt Restriction

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Abstract
Lifestyle improvement is a cornerstone of cardiovascular disease prevention and has a relevant effect on blood pressure control. During the last decades the attention of the researcher has focused on low-salt diets as the lifestyle modification most effective in blood pressure reduction. Current international guidelines thus suggest to stress the importance of the implementation of the dietary approach to stop hypertension (DASH) diet and of a low-salt Mediterranean diet to achieve the best results in term of blood pressure decrease. However, salt reduction in diet could be not the only nor the main determinant of blood pressure reduction under dietary treatment. DASH and low-salt Mediterranean diet are also characterized by a high intake of vegetables (NO and polyphenol sources), whole grains, some low-fat dairy products, and low intake of red meat, sugar, and trans-hydrogenated fats. Lacto-ovo vegetarian diet are also per se associated to a significant improvement in blood pressure levels. Moreover, these diets are particularly effective when associated with a significant weight loss. Furthermore, blood pressure can also be lowered by some nutraceuticals (beetroot, magnesium, vitamin C, catechin-rich beverages, lycopene, etc). The aim of this narrative review is to critically resume the most recent evidence supporting a complete approach to dietary counseling for hypertension prevention and management.

Keywords  Diet · Blood pressure · Dietary supplements · Hypertension · Lifestyle

1 Introduction
Lifestyle improvement is a cornerstone of cardiovascular disease prevention and diet is one of the most effective strategy for attaining on blood pressure (BP) reduction and control [1].

During the last decades the attention of the researcher has focused on low-salt diets as the most effective lifestyle modification in BP reduction. In fact, from an epidemiological point of view is known that a daily intake of sodium > 5 g is associated with a proportional increase in systolic BP, both in children [2] and in adults [3], whereas it has been estimated (but not proven) that daily intake > 2 gr is associated to more than 1 of every 10 deaths from cardiovascular causes [4].

This could be mainly due to the fact that dietary sodium restriction has a significant BP-lowering effect. A very recent and huge meta-analysis of 85 trials, mainly carried out on hypertensive patients, with sodium intake ranging from 0.4 to 7.6 g/day and follow-up from 4 weeks to 36 months, showed an approximately linear relationship between sodium intake and increase in both systolic and diastolic BP across the entire range of dietary sodium exposure [5]. Another meta-analysis of 17 cohorts with 457 participants showed that salt restriction was associated with a significant reduction in augmentation index (9.3%) as well as central systolic BP and central pulse pressure [6]. Then, an average reduction in sodium intake of 89.3 mmol/day was associated with a 2.84% (95% CI 0.51–5.08) reduction in carotid-femoral pulse wave velocity [7].

On the other side, quick dietary sodium restriction has been associated with significant increase in serum renin, noradrenalin, adrenalin, and heart rate, and a mild but
significant impairment in plasma lipid levels [8, 9]. For these reason, and in order to consent the patient adaption to the lower food sapidity, at the stage of hypertension diagnosis a mild and progressive reduction of salt intake should be suggested in spite of a quick and dramatic cut of salt assumption. The antihypertensive effect of sodium restriction is more pronounced in people of African descent, in older patients, and patients with diabetes, metabolic syndrome, or chronic kidney disease [10], but less pronounced in young overall health caucasians. Moreover, salt restriction could not be always easy, as often it is hidden in processed foods. Finally, it is not so evident that long-term dietary sodium restriction is associated to a significant reduction in cardiovascular disease risk [11].

In this context, there is a growing interest for implementation of whole dietary patterns or single nutrients other than sodium and nutraceuticals potentially improving BP control.

2 Dietary Patterns Improving Blood Pressure Control

Different dietary patterns have proven an effective BP lowering effect (Fig. 1).

– The dietary approach to stop hypertension (DASH) diet

The DASH diet is an overall healthy low-salt diet high intake of vegetables, whole grains, some low-fat dairy products, and low intake of red meat, sugar, and trans-hydrogenated fats, when compared to a standard Western diet [12].

Compared to the typical North-American diet, the DASH one is associated with lower systolic BP independently from the sodium intake and with lower diastolic BP in subjects with intermediate-high sodium intake: the mean systolic BP fell by 7.1 mmHg in normotensive subjects, and by 11.5 mmHg in hypertensive patients [13].

A recent meta-analysis of 17 trials showed a significant preventive effect of DASH diet on mortality for different causes with hazard rations 0.95 (95% CI 0.94–0.96, I² = 91.6%) for all-cause, 0.96 (95% CI 0.95–0.98, I² = 82.4%) for cardiovascular diseases, 0.97 (95% CI 0.96–0.98, I² = 0.00%) for stroke, and 0.97 (95% CI 0.95–0.98, I² = 63.7%) for cancer mortality per each 5-point increment of adherence to the DASH diet [14]. DASH diet would also reduce the risk to develop type 2 diabetes (RR = 0.82; 95% CI 0.74–0.92) [15].

– The Mediterranean diet

The Mediterranean diet is based on the traditional dietary pattern of old Greece and southern Italy, being rich in fruits, vegetables, legumes, cereals, dairy products (cheese, yogurt), fish, olive oil, and with small amount of wine and lean meats. The main differences with the DASH diet is related to the attention to the seasonality of fresh foods, the large number of polyphenols containing foods (in particular olives and extravirgin olive oil) and the use of vegetable oils in spite of animal oils, when compared with other traditional diets [16]. The Mediterranean diet has a less significant impact on BP than DASH-diet, probably because it is not strictly a low-salt diet. Another reason is related to the fact that a part of the available trials compared the effect of high adherence to low adherence to Mediterranean diet in Mediterranean countries (in particular Italy and Spain) where the low adherence is represented by a dietary pattern that is always healthier than the one in North-Europe or North-America [17]. This attenuate the measured effect of Mediterranean diet on BP. A recent umbrella meta-analysis of 57 trials involving 36,983 participants concluded that adherence to the Mediterranean diet is able to improve anthropometric measurements, BP, insulin-resistance, lipid pattern, liver transaminases and hepatic fat mass, systemic inflammation, flow-mediated dilatation and the risk of cardiovascular disease incidence (risk ratio = 0.61, 95% CI 0.42–0.80; I² = 0%), and stroke (risk ratio = 0.67, 95% CI 0.35–0.98; I² = 0%) [18]. However, the available evidence suggest that Mediterranean diet is associated to a mildly reduced risk of cardiovascular disease both in primary and secondary prevention setting, but the quality of the evidence is not so good and a definitive conclusion can not be currently drawn [19]. One more time, a part of the available trials compared the effect of high adherence to low adherence to Mediterranean diet in Mediterranean countries where the low adherence is represented by a dietary pattern that is always healthier than the one in North-Europe or North-America and where the baseline cardiovascular risk is meanly low, so that a risk...
reduction is less easily detectable. On the other side, adherence to the Mediterranean diet is associated to improved a significant reduction in the risk of all-cause mortality (relative risk for the study-specific highest/lowest and per 1sd MDS increment 0.79 (95% CI 0.77, 0.81, $I^2 = 42\%$) and 0.92 (95% CI 0.90, 0.94, $I^2 = 56\%$), respectively) [20].

Vegetarian and vegan diets

A huge meta-analysis of long-term studies (n = 118,518; 2,936,359 person-years of follow-up) showed a positive association between meat (including poultry) and risk to develop hypertension, independently from fruit, vegetable, and whole grain intake [21]. On the contrary, a recent meta-analysis of 41 clinical trials (8416 participants) comparing different plant-based diet showed that lacto-ovo vegetarian diet has a significant BP effect lowering effect, while vegan not (systolic BP: $-5.47$ mmHg (95% CI $-7.60, -3.34$) vs. $1.30$ mmHg (95% CI $-3.90, 1.29$). Similar effects were seen on diastolic BP, as well [22]. Vegetarian diets are also protective against the development of type 2 diabetes; odds ratio for diabetes in vegetarians vs. non-vegetarians was 0.73 (95% CI 0.61, 0.88) [23].

Vegetarian diets are associated with reduced risk of all-cause mortality, and in particular of mortality due to cardiovascular (0.92, 95% CI 0.85, 0.99; $I^2 = 0\%$) and coronary artery disease (0.76; 95% CI 0.68, 0.85; $I^2 = 35\%$) [24]. It has yet to be fully elucidated which subtype of vegetarian diet (vegan, lacto-vegetarian, lacto-ovo vegetarian, pescovegetarian) could have the best BP lowering and cardiovascular disease prevention effect.

On the other side, the vegetarian and vegan diet-related deficit of vitamin B12 intake could reduce their potential positive impact on cardiovascular disease prevention [25]. Then, compared with omnivores, vegetarians and vegans had lower BMD at the femoral neck and lumbar spine and vegans also had higher fracture rates [26]. Moreover, vegetarians show higher depression scores than non-vegetarians [27].

Low-energy diets

Increased body weight and obesity are the independent risk factors for hypertension [28].

A meta-analysis of 8 clinical trials involving 2100 patients showed a significant BP reduction in participants assigned to weight-loss diets as compared to controls: systolic BP: mean difference (MD) $-4.5$ mm Hg (95% CI $-7.2$ to $-1.8$ mm Hg), and diastolic BP: MD $-3.2$ mm Hg (95% CI $-4.8$ to $-1.5$ mm Hg) [29]. A further metaanalysis showed that body weight loss is also associated to a significant reduction in heart rate ($-9$ beats/min, 95% CI $-12$ to $-6$; $p < 0.001$), resting oxygen consumption ($-85$ ml/min, 95% CI $-111$ to $-60$; $p < 0.001$) and mean pulmonary artery pressure ($-5$ mm Hg, 95% CI $-8$ to $-2$; $p = 0.001$) [30].

Energy restriction could be obtained in different ways. In general, caloric restriction can lower both systolic BP and diastolic BP regardless of sex, ethnic group, BMI, presence of metabolic syndrome, or diabetes mellitus. BP-lowering effect may continue beyond the end of the fasting period. The greatest decrease takes place in patients with the highest baseline BP [31].

Alternate-day fasting has an increased popularity and is associated with an improvement of anthropometric measurements, glucose metabolism, lipid pattern and blood pressure [32].

Very low carbohydrate ketogenic diets (VLCKD) are associated with a quick and impressive reduction in body weight and BP (systolic BP $-8$ mmHg, diastolic BP $-7$ mmHg) [33]. The available studies are relatively short, but the most part of VLCKD protocols are of short duration and aim to train the subjects to a more healthy and balanced diet after some months of energy restriction. This approach could be more indicated in obese subjects resistant to previous dietary approaches [34].

Low-energy diets have been mainly tested in overweight-obese patients, so that it is not yet clear their potentially efficacy in lean hypertensive subjects, in particular when affected by insulin-resistance.

Other dietary patterns

Paleolithic type diet (nutrition of preagricultural hunter-gatherers including lean meat, fruits, vegetables, and nuts, while avoiding intake of grains, dairy products, processed foods, and added sugar and salt) led to the significant improvement of both systolic (WMD $-4.24$ mm Hg; 95% CI $-7.11, -1.38$ mm Hg) and diastolic (WMD $-2.95$ mm Hg; 95% CI $-4.72, -1.18$ mm Hg) BP, without relevant impact on body weight [35].

Among other popular diets, the Atkins (systolic BP$-5.1$ mm Hg, diastolic BP$-3.3$ mm Hg) and the Zone (systolic BP $3.5$ mm Hg, and diastolic BP $2.3$ mm Hg) also exerted a significant BP reduction effects [36]. Both diets are associated with body weight loss and have not studied on the long-term.

Nutraceuticals

Some single natural molecules are associated with a significant improvement in BP under controlled dietary conditions. In this context, recently, both the Italian [37] and the European Hypertension Societies [38] published statements related to the best available evidence of efficacy for some of them.
Both documents conclude that a sufficient clinical evidence of efficacy and safety exist for dietary supplementation with beetroot juice, magnesium, vitamin C, and catechin-rich beverages. Soy isoflavones could be suggested in perimenopausal women, resveratrol—in insulin-resistant patients, melatonin—in the subjects with nocturnal hypertension. Even if potassium is one of the most effective antihypertensive nutraceutical, warning on potassium intake is needed in patients with advanced chronic kidney failure and those assuming potassium-sparing diuretics/antialdosteroneics. Pomegranate juice, karkadè tea and sesame effectiveness has been demonstrated in Middle-East people [37, 38]. Lactotripeptides are effective only in Asian people [39], while polyunsaturated fatty acids from fish exert small effect on BP [40]. The possible additive effect of the combination of some of them is promising and under investigation [41].

### 3 Discussion

One of the first scientific attempt to manage heart failure and hypertension with diet is due to Kempner in the late 1930s. In fact he proposed to use a rice-based diet as a treatment for a patient with renal failure and congestive heart failure. He showed that this intervention led to the decrease of heart size according to the chest X-ray, normalization of ECG, and improvement of retinal conditions. Then, Kempner obtained similar results in a cohort of hypertensive patients: rice and fruit diet helped them to significantly decrease their BP and heart size. Sadly, these findings did not receive enough attention from the scientific community [42].

The modern pre-pharmacological approach to prevention and management of hypertension should be multitarget, suggesting improvement of body weight, quality of diet and eventually inclusion of some dietary supplements.

The main international guidelines for the management of hypertension follows this approach (Table 1). Guidelines for the prevention, detection, evaluation, and management of high BP in adults, issued by American College of Cardiology/American Heart Association (2017) recommend a heart-healthy diet, that could be resumed in the DASH diet [43]. Guidelines for the management of arterial hypertension, issued by European Society of Cardiology/European Society of Hypertension (2018), support the suggestion of a low-salt Mediterranean-like diet [44]. On May 2020, the International Society of Hypertension issued Global Hypertension Practice Guidelines, which recommend a DASH-like diet, also highlighting the possible BP lowering effect of vegetables sources of nitrates like beetroot and leafy vegetables. Moreover, they also cited foods rich in calcium, magnesium, and potassium (avocados, nuts, seeds, legumes, and tofu) as having some antihypertensive benefits [45].

The dietary supplementation with beetroot juice, magnesium, vitamin C, and catechin-rich beverages could further improve BP control [46].

The antihypertensive effect observed with the above cited diet is sometime huge and similar to that achieved with the best pharmacological treatment, however the long-term compliance and consequently the long-term efficacy of these diet has yet to be rigorously quantified.

In conclusion, combining data derived by the available literature, we should propose a low-salt energy-restricted Mediterranean diet to the most part of our overweight hypertensive patients. In some cases (obese subjects apparently resistant to standard diets) VLCKD could be considered. Physical sactivity increase and smoking cessation should also always suggested [47]. This approach could prevent the use of antihypertensive drugs, reduce the dose or number of drugs employed, and improve the efficacy of the pharmacological treatment. Moreover, it would have a global positive impact on the cardiovascular risk profile both of patients in primary and secondary prevention for cardiovascular diseases.

### Declarations

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