An evidence-based appraisal of complementary and alternative medicine strategies for the management of hypertension

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Hypertension is a major risk factor for cardiovascular disease and all-cause mortality. Numerous antihypertensive medications and lifestyle changes have proven effective for the reduction of blood pressure (BP). Over the past few decades, the emergence of complementary and alternative medicine (CAM)-based strategies to lower BP have broadened the therapeutic armamentarium for hypertension. CAM is defined as a group of heterogeneous medical treatments that are used to enhance the effect of standard therapy, or, conversely, are implemented as an alternative to standard practice. The available body of evidence does substantiate the BP-lowering effects of certain CAM-based therapies in individuals with and without established hypertension. Collectively, alternative strategies for BP reduction have undergone less rigorous testing than traditional BP-lowering strategies and the lack of robust clinical data has greatly hampered the broad-scale adoption of CAM therapies into clinical practice. Despite these limitations, CAM-based therapies for the reduction of BP require consideration as they could offer substantial public health benefits given the high prevalence of hypertension in the general population. This article reviews some of the most promising CAM-based therapies for the reduction of BP and cardiovascular outcomes based on the current literature.

Keywords: blood pressure, cardiovascular disease, hypertension

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; CAM, complementary and alternative medicine; DHA, docosahexaenoic acid

INTRODUCTION

Hypertension is the most prevalent modifiable risk factor for cardiovascular disease. Thiazide diuretics, angiotensin-converting enzyme inhibitors/angiotensin receptor blocker, and dihydropyridine calcium-channel blockers constitute the cornerstone of antihypertensive drug management owing to their clinical efficacy and established role in reducing incident cardiovascular disease. Despite increasing disease awareness, the prevalence of uncontrolled hypertension remains high. In fact, according to the 2017 American College of Cardiology/American Heart Association (ACC/AHA) Guidelines, over 50% of US adults who are taking antihypertensive medications are not achieving blood pressure (BP) goals [1]. This dichotomy illustrates the tremendous challenges of achieving BP control across diverse patient populations.

Complementary and alternative medicine (CAM) is a group of diverse therapeutic medical treatments that are generally not considered the standard of practice. Complementary medicine is used in conjunction with conventional therapies, whereas alternative medicine is used in lieu of conventional therapies. Integrative medicine combines conventional and CAM treatments for which there is evidence of safety and effectiveness. BP guidelines have not promulgated broad scale implementation of CAM-based therapies to lower BP. This lack of endorsement is due to lower quality data compared with pharmacologic and lifestyle modification treatments. Nonetheless, the use of CAM remains popular. In the United States, approximately 38% of adults are currently using CAM-based therapies [2]. Moreover, nearly 80% of patients perceived the combination of CAM and their physicians' treatment to be superior to either therapy alone [3]. In a scientific statement from the AHA in 2013, the consensus of the writing group was that it is reasonable for all individuals with BP levels more than 120/80 mmHg to consider a trial of complementary/alternative approaches as an adjuvant method to help lower BP [4].

Integrative approaches to the management of hypertension may help overcome some of the obstacles to achieving optimal BP control. CAM strategies represent a promising and attractive adjunct to traditional BP reduction strategies. The incorporation of CAM is an additional tool that physicians can utilize to achieve BP control and sustain that control over time. The widespread implementation of CAM-based treatment options for the reduction of BP has been

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hampered by the lack of strong clinical data supporting its clinical efficacy and safety. With respect to cardiovascular disease, the landscape of CAM-based therapies may be shifting, as some recent randomized controlled trials involving CAM-based therapies have demonstrated reduction in major cardiovascular endpoints in select populations [5,6]. A thorough understanding of CAM, as it relates to hypertension management, can help the physician guide their patients with hypertension toward a successful treatment strategy that integrates all facets of BP-lowering techniques. This article provides an evidence-based appraisal of the most widely used CAM therapies for the reduction of BP and explores the impact of such BP reduction on cardiovascular events.

VITAMIN D

Vitamin D may play an integral role in BP regulation and cardiovascular disease. Experimental data in both animal and human models have implicated a role of vitamin D in BP regulation. Renin-angiotensin system (RAS) activity inhibition, improved calcium homeostasis, and direct effect on vascular endothelium and smooth muscle have all been implicated as the mechanistic link between vitamin D and BP [7–10] and these effects contribute to the development of cardiovascular disease (Fig. 1).

Observational studies have consistently demonstrated an inverse relationship between BP and 25(OH)D levels. In the National Health and Nutrition Examination Survey III study, the average SBP was nearly 3 mmHg lower in volunteers with the highest quartile of 25(OH)D compared with volunteers in the lowest quartile [12]. Forman *et al.* [13] examined the impact of vitamin D status on incident hypertension among young women. In this study, 1811 nonhypertensive participants were followed for 4 years. Those with 25(OH)D levels less than 15 ng/ml had a relative risk (RR) for incident hypertension of 2.67 [95% confidence interval (CI): 1.05–6.79] compared with those whose levels were above 30 ng/ml after adjusting for several demographic and lifestyle factors. The same authors then performed a nested case–control study within the Nurses' Health Study II cohort and, after adjustment for various confounders, they observed an odds ratio (OR) for incident hypertension of 1.66 (95% CI: 1.11–2.48) comparing the lowest (less than 21.0 ng/ml) with highest (above 32.3 ng/ml) quartile of 25(OH)D (P for trend = 0.01) [9]. These results were confirmed by Jorde *et al.* who found that individuals whose baseline 25(OH)D level was less than 16.6 ng/ml had an adjusted OR for incident hypertension of 1.22 (95% CI: 0.87–1.72) [14].

As the prevalence of vitamin D insufficiency in certain US populations exceed 80%, correction of vitamin D deficiency as a therapy for BP control would have a major impact on BP control rates [14]. On the contrary, the preponderance of randomized controlled trials (RCTs) have failed to support the antihypertensive effects of vitamin D supplementation [15,16]. The Styrian Vitamin D Hypertension Trial was a single-center, double-blind, placebo-controlled study conducted from June 2011 to August 2014 at the endocrine outpatient clinic of the Medical University of Graz, Austria

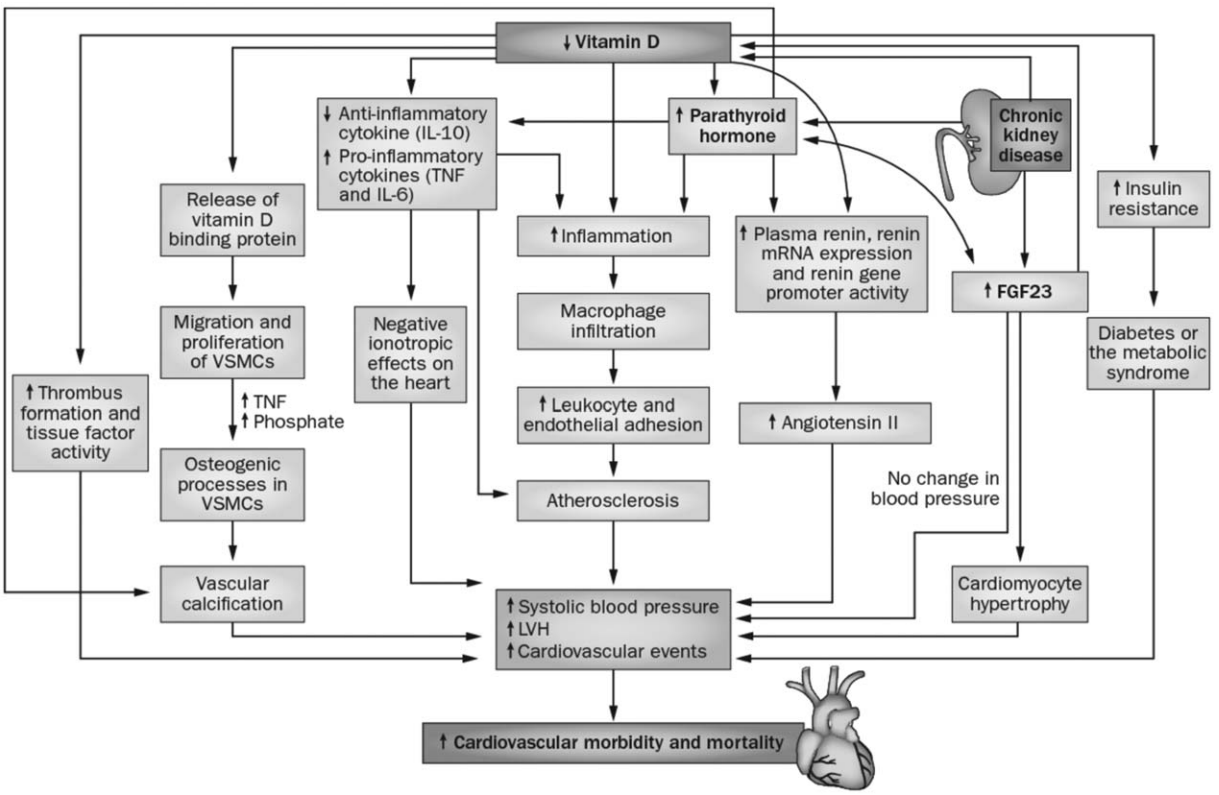

FIGURE 1 Vitamin-D-related pathways that contribute to cardiovascular morbidity and mortality. A decreased serum level of vitamin D is a risk factor for cardiovascular morbidity and mortality owing to increases in SBP, left ventricular hypertrophy (LVH), and adverse cardiovascular events [11].

[17]. The study enrolled 200 study participants with arterial hypertension and 25-hydroxyvitamin D levels below 30 ng/ml. Study participants were randomized to receive either 2800 IU of vitamin D3 per day as oily drops ($n = 100$) or placebo ($n = 100$) for 8 weeks. Primary outcome measure was 24-h SBP. A total of 188 participants [mean (SD) age, 60.1 (11.3) years; 47% women; 25-hydroxyvitamin D, 21.2 (5.6) ng/ml] completed the trial. The mean treatment effect did not reach statistical significance.

The response to vitamin D supplementation may vary depending on race. Blacks in the United States have significantly higher rates of hypertension and lower circulating levels of 25 vitamin D, compared with whites [18]. Forman *et al.* [19] performed a randomized controlled trial examining the effect of vitamin D on BP in healthy African-Americans without established hypertension. During two winter periods from 2008 to 2010, 283 African-Americans were randomized into a four-arm, double-blind trial for 3 months of placebo, 1000, 2000, or 4000 IU of cholecalciferol per day. At baseline, 3 months, and 6 months, systolic and diastolic pressure and 25-hydroxyvitamin D were measured. The difference in systolic pressure between baseline and 3 months was +1.7 mmHg for those receiving placebo, −0.66 mmHg for 1000 U/day, −3.4 mmHg for 2000 U/day, and −4.0 mmHg for 4000 U/day of cholecalciferol (−1.4 mmHg for each additional 1000 U/day of cholecalciferol; $P = 0.04$). For each 1 ng/ml increase in plasma 25-hydroxyvitamin D, there was a significant 0.2 mmHg reduction in systolic pressure ($P = 0.02$). There was no effect of cholecalciferol supplementation on diastolic pressure ($P = 0.37$). Within an unselected population of African-Americans, 3 months of oral vitamin D3 supplementation significantly, yet modestly, lowered systolic pressure. As seen in many other facets of BP, race may play a pivotal role and may predict the response to therapeutic interventions, including vitamin D.

The majority of observational data demonstrate a strong correlation between low vitamin D levels, elevated BP, and risk of developing hypertension. Similarly, experimental studies in both animals and humans imply a definitive role of vitamin D in the BP regulation. On the contrary, randomized controlled trials have not uniformly demonstrated a BP-lowering effects of vitamin D supplementation. More studies are required to determine whether vitamin D supplementation can be an effective strategy to lower BP and prevent incident hypertension.

MAGNESIUM

Magnesium may play an integral role in the prevention and control of hypertension. Basic science research has elucidated several proposed mechanisms for the BP-lowering effects of magnesium. These mechanisms include nitric oxide and prostaglandin synthesis, modulation of endothelial vasodilation, decreased vascular tone and reactivity, and its antioxidant properties [20–22]. Observational studies have shown a significant inverse linear effect between magnesium levels and incidence of hypertension [23]. When comparing the highest to lowest magnesium levels, the pooled RR of incident hypertension was 0.91 (95% CI: 0.8, 1.02, $P = 0.10$) in this population. In addition, low-dietary magnesium intake may be associated with higher risk of incident hypertension. A systematic review and meta-analysis of prospective cohort studies performed by Han [24] demonstrated a statistically significant inverse association between dietary magnesium intake and the risk of hypertension. For a 100 mg/day increase in dietary magnesium intake, the risk of developing hypertension decreased by 5%. Zhang and Li [25] attempted to quantify the effect of oral magnesium supplementation on BP in both normotensive and hypertensive patient populations. In this meta-analysis of RCTs, the authors noted a moderate reduction in SBP by 2 mmHg (95% CI: 0.43–3.58) and DBP by 1.78 mmHg (95% CI: 0.73–2.82). This BP-lowering effect occurred at a median magnesium dose of 368 mg/day over a median of 3 months. The BP-lowering effect occurred despite only modest changes in serum magnesium levels. High-dietary magnesium intake and magnesium supplementation seem to have favorable effect on BP levels. On the contrary, the studies have not been consistent and are not of sufficient quality to make firm conclusions. Further research is necessary to solidify the role of magnesium in the management of hypertension.

CALCIUM

Experimental data suggest a link between calcium and BP regulation [26,27]. Currently, there is a dearth of clinical data examining the BP effect of elemental calcium supplementation alone. Consequently, most of the clinical data on elemental calcium supplementation is extrapolated from data studying coadministration of calcium and vitamin D. The Women's Health Initiative Calcium/Vitamin D Trial randomly assigned 36 282 postmenopausal women to receive 1000 mg of elemental calcium and 400 IU of vitamin D3 daily or placebo in a double-blind fashion [28]. Over a median follow-up time of 7 years, there was no significant difference in the mean change over time in SBP (0.22 mmHg; 95% CI: −0.05–0.49 mmHg) and DBP (0.11 mmHg; 95% CI: −0.04–0.27 mmHg) between the active and placebo treatment groups. In 17 122 nonhypertensive participants at baseline, the hazard ratio for incident hypertension associated with calcium/vitamin D treatment was 1.01 (95% CI: 0.96–1.06). In a recent meta-analysis that included male and female participants, Wu and Sun [29] found no difference in daytime office BP readings associated with calcium and vitamin D supplementation. Further research is required to establish a role for elemental calcium supplementation for BP management, especially since calcium supplementation does increase the risk of nephrolithiasis [30].

The role of elemental calcium supplementation for hypertensive disorders in pregnancy are more clearly delineated. Belizan [31] studied 1194 nulliparous women who were in the 20th week of gestation at the beginning of the study. The women were randomly assigned to receive 2 g/day of elemental calcium or placebo. The rates of hypertensive disorders of pregnancy were lower in the calcium group than in the placebo group (9.8 vs. 14.8%; OR, 0.63; 95% CI: 0.44–0.90) and less of an increase in SBP and DBP than placebo. The risk of these hypertensive disorders was lower at all times of gestation. The WHO currently recommends elemental calcium supplementation in pregnant

women with low-dietary calcium intake to reduce the risk of pre-eclampsia [32].

COENZYME Q10

Coenzyme q10 (CoQ10) is known as ubiquinone because of its ubiquitous distribution in nature. CoQ10 is an antioxidant and plays a major role in the mitochondrial respiratory chain for energy production [33]. Experimental studies have demonstrated the primary action of CoQ10 in clinical hypertension is vasodilatation, via a direct effect on the endothelium and vascular smooth muscle [34,35]. Observational data has suggested CoQ10 deficiency is a potential risk factor for the development of hypertension [36]. Rosenfeldt and Haas [37] performed a meta-analysis examining the impact of CoQ10 supplementation on BP control. A total of 12 clinical trials (362 patients) comprising three randomized controlled trials, one crossover study and eight open-label studies were included in the meta-analysis. In the randomized controlled trials ($n = 120$), SBP in the treatment group was 167.7 (95% CI: 163.7–171.1) mmHg before, and 151.1 (147.1–155.1) mmHg after treatment, a decrease of 16.6 (12.6–20.6, $P < 0.001$) mmHg, with no significant change in the placebo group. DBP in the treatment group was 103 (101–105) mmHg before, and 94.8 (92.8–96.8) mmHg after treatment, a decrease of 8.2 (6.2–10.2, $P < 0.001$) mmHg, with no significant change in the placebo group. In the crossover study ($n = 18$), SBP decreased by 11 mmHg and DBP by 8 mmHg ($P < 0.001$) with no significant change with placebo. In the open-label studies ($n = 214$), mean SBP was 162 (158.4–165.7) mmHg before, and 148.6 (145–152.2) mmHg after treatment, a decrease of 13.5 (9.8–17.1, $P < 0.001$) mmHg. Mean DBP was 97.1 (95.2–99.1) mmHg before, and 86.8 (84.9–88.8) mmHg after treatment, a decrease of 10.3 (8.4–12.3, $P < 0.001$) mmHg. The side effects in the treatment groups were minimal. All three types of study (randomized controlled, crossover, and open label) showed decreases in SBP ranging from 11 to 17 mmHg and in DBP ranging from 8 to 10 mmHg. Of all the CAM-based strategies discussed in this article, CoQ10 supplementation exhibits the greatest magnitude of BP reduction and merits consideration as an adjunctive therapy in most patients with hypertension.

In addition to its effect on BP, CoQ10 supplementation appears to reduce major adverse cardiovascular events in select populations. The Q-SYMBIO trial was a prospective, randomized, double-blinded, placebo-controlled, multicenter trial of CoQ10 as an adjunctive treatment for individuals with chronic heart failure [5]. The majority of patients enrolled in this study were on antihypertensive agents during the study period. In this study, the total number of cardiovascular deaths within the study period of 106 weeks was lower in the CoQ10 group ($n = 18$, 9%) compared with the placebo group ($n = 34$, 16%), corresponding to a 43% RR reduction ($P = 0.039$). There were 21 deaths (10%) from all causes in the CoQ10 group compared with 39 deaths (18%) in the placebo group with hazard ratio of 0.51 ($P = 0.018$, Fig. 2). In clinical practice, the administration of CoQ10 in the subset of hypertensive patients with heart failure, may amplify the magnitude of cardiovascular benefit and is a safe and easy to implement strategy. A high-quality, prospective, randomized controlled trial examining the cardiovascular benefits of CoQ10 in the hypertensive population remains elusive.

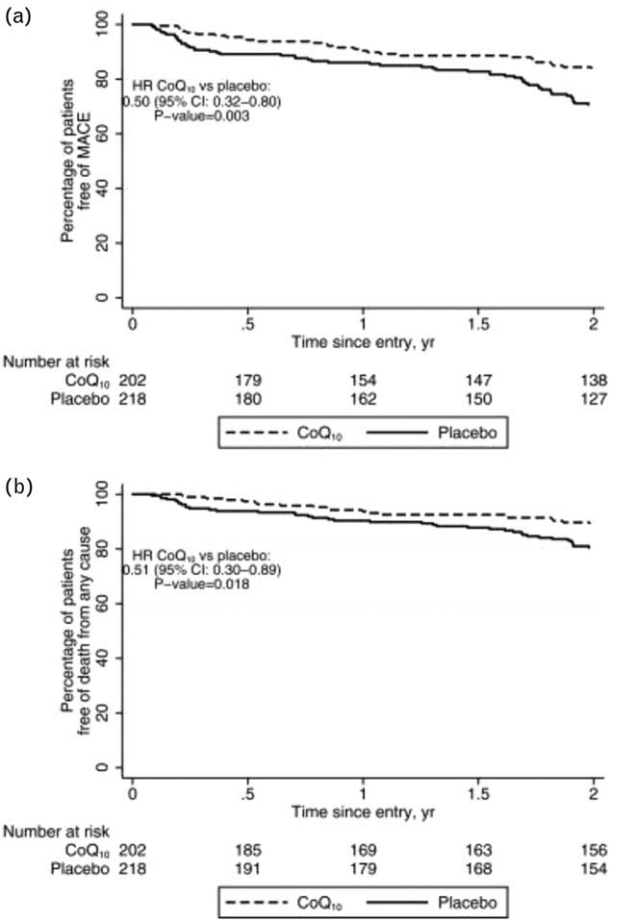

FIGURE 2 Kaplan–Meier estimates of the time to primary and secondary endpoints. Kaplan–Meier estimates of the time to the primary endpoint major adverse cardiovascular events (a) and the secondary outcome death (b) in the placebo group (solid line) and the coenzyme Q10 group (dashed line). The primary endpoint was composite major adverse cardiovascular event of hospital stay for worsening heart failure, cardiovascular death, mechanical support, or urgent cardiac transplantation. A specified secondary outcome was death from any cause. CI, confidence interval; HR, hazard ratio.

GARLIC

Garlic (*Allium sativum*) has been used for thousands of years for medicinal purposes. Garlic supplements have been linked to improved cardiovascular health, including reduction in BP [38]. Garlic contains a compound called allicin, which is a sulfur-containing compound that has been reported to modulate endothelium through the production of nitric oxide [39–41]. A recent meta-analysis was performed by Wang *et al.* [42] to investigate the effect of garlic on BP. The meta-analysis included 20 trials with 970 patients, including hypertension and normotensive participants in garlic and placebo groups. It showed a mean decrease in SBP of 5.1 ± 2.2 mmHg ($P < 0.001$) and a mean decrease DBP of 2.5 ± 1.6 mmHg ($P < 0.002$) compared with placebo. Subgroup analysis of trials in hypertensive individuals at baseline revealed a larger significant reduction in SBP of 8.7 ± 2.2 mmHg ($P < 0.001$; $n = 10$) and DBP

of 6.1 ± 1.3 mmHg ($P < 0.001$, $n = 6$). In the analysis investigating dose–response relationship, the dosage of garlic powder in the studies ranged from 300 to 2400 mg/day and the duration of intervention ranged from 2 to 24 weeks. There were two studies that investigated multiple levels of garlic intake. The maximum antihypertensive effect of garlic was produced at 480-mg garlic at week 12. The study has limitations. Low sample size, study heterogeneity, and different garlic supplements are some of the limitations of this particular meta-analysis. Garlic has been used for reported antithrombotic properties, but studies have not consistently demonstrated excessive bleeding risk as a safety concern [43].

CACAO

The potential salutary effects of chocolate consumption originated from observations in population studies of Kuna Indians [44]. Kuna Indians in Panama consume 10 times more cocoa than those in Panama and have ~80% less cardiovascular disease and a low prevalence of hypertension despite a high-sodium diet [44]. By comparison, Kuna Indians that migrate to Panama manifest age-dependant increased in BP and a higher prevalence of hypertension than Kuna Indians. On the basis of this observation, Corti *et al.* [45] proposed that flavanols, especially epicatechin, was the compound in cocoa responsible for the lower BP.

A meta-analysis on cocoa and BP identified five studies of adequate quality for inclusion [46]. In these reports, cocoa lowered SBP 4.7/2.8 mmHg ($P = 0.002/0.006$). In another meta-analysis that included these five studies and eight additional peer-reviewed studies, dark chocolate lowered SBP in six of seven open-label studies, but DBP in only one of six double-blind studies [47–49]. Because cocoa lowered BP in open-label, but not double-blind studies, consideration for placebo effect must be considered. In addition, variations in BP measurement and the use of different chocolate manufacturers make firm conclusions regarding the effect of cocoa on BP difficult to assess.

OMEGA 3

Omega-3 fatty acids (FAs) have garnered some attention for reported BP-lowering effects. The active ingredients of fish oil considered responsible for its antihypertensive effect are the long-chain omega-3 FAs eicosapenaenoic acid and docosahexaenoic acid (DHA) [50]. A meta-analysis of seventy RCTs compared BP-lowering effect of placebo vs. eicosapentaenoic acid (EPA) + DHA provision [51]. EPA + DHA reduced SBP 1.52 mmHg (95% CI: −2.25 to −0.79) and DBP 0.99 mmHg (95% CI: −1.54 to −0.44). The strongest effect of EPA + DHA was observed among untreated hypertensive individuals (SBP −4.51 mmHg and DBP −3.05 mmHg), although the BP was lowered in normotensive individuals (SBP −1.25 mmHg and DBP −0.62 mmHg). There was no clear pattern of dose–response between EPA + DHA and SBP. Significant reductions were observed with doses of 1 to less than 2 g/day (−1.81 mmHg) and 3 to less than 4 g (−3.85 mmHg). No apparent effect on DBP was observed for dose levels less than 2 g/day, whereas significant reductions were observed for 2 to less than 3 g/day (−1.09 mmHg) and 3 to less than 4 g/day (−1.86 mmHg). The results from this analysis demonstrate that EPA + DHA are as effective, and in some cases are more effective, than other lifestyle-related interventions, including increasing physical activity and restricting alcohol and sodium, for lowering BP among hypertensive populations not taking antihypertensive medications.

Increased intake of omega-3 FAs has been associated with reduced risk of cardiovascular disease in observational studies [52,53]. Until recently, large randomized controlled trials examining the cardiovascular benefit of omega-3 FAs have been lacking. In the recently published A Study of Cardiovascular Events in Diabetes Trial, patients with diabetes and without evidence of cardiovascular disease, were randomized to receive omega-3 supplements or placebo [54]. About half of the study participants had enrollment SBP equal to or greater than 130 mmHg. After a mean follow-up of 7.4 years, there was no statistical difference in the primary end point of serious vascular events [nonfatal myocardial infarction (MI), stroke, transient ischemic attack (TIA), or death from vascular cause, $P = 0.55$]. In the recently released Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial (REDUCE-IT), patients with hypertriglyceridemia and either cardiovascular disease (CVD) or diabetes mellitus were randomized to icosapent ethyl or placebo [55]. Icosapent ethyl (vascepa) is a highly purified ethyl ester of EPA. The primary cardiovascular outcome of cardiovascular death, nonfatal MI, stroke, coronary revascularization, or unstable angina, for icosapent ethyl vs. placebo, was 17.2 vs. 22% (hazard ratio 0.75, CI 0.68–0.83, $P < 0.0001$, Fig. 3). These recent studies show conflicting results regarding the cardiovascular protection of omega-3 FAs, indicated that the formulation and dose of fish oil may have variable results on cardiovascular outcomes.

In a recent meta-analysis, marine omega-3 supplementation lowered the risk of MI, coronary heart disease (CHD) death, total CHD, CVD death, and total CVD, event after exclusion of REDUCE-IT [56]. A stronger inverse association for these outcomes was demonstrated when REDUCE-IT was included in the analysis. Also, the authors noted a linear dose–response relationship between marine omega-3 supplementation and several CVD end points. Applying these results to clinical practice, it may not be one size fits in regards to fish oil. The dose and formulation of fish oil may be a major determinant of the magnitude of BP reduction and cardiovascular risk reduction.

ACUPUNCTURE

Acupuncture has been postulated to reduce BP for decades. The mechanism of the BP-lowering effect is generally considered to be attenuation of sympathetic nervous system activation through stimulation of mechanoreceptors and nociceptors [57]. In a meta-analysis performed in 2009, eleven RCTs were analyzed to estimate the effect of acupuncture on BP in hypertensive patients [58]. Three sham-controlled trials out of the eleven studies were statistically pooled. SBP change was not statistically significant ($P = 0.12$) and acupuncture only marginally reduced DBP by 3 mmHg ($P = 0.05$), but substantial heterogeneity was observed. When acupuncture was performed with

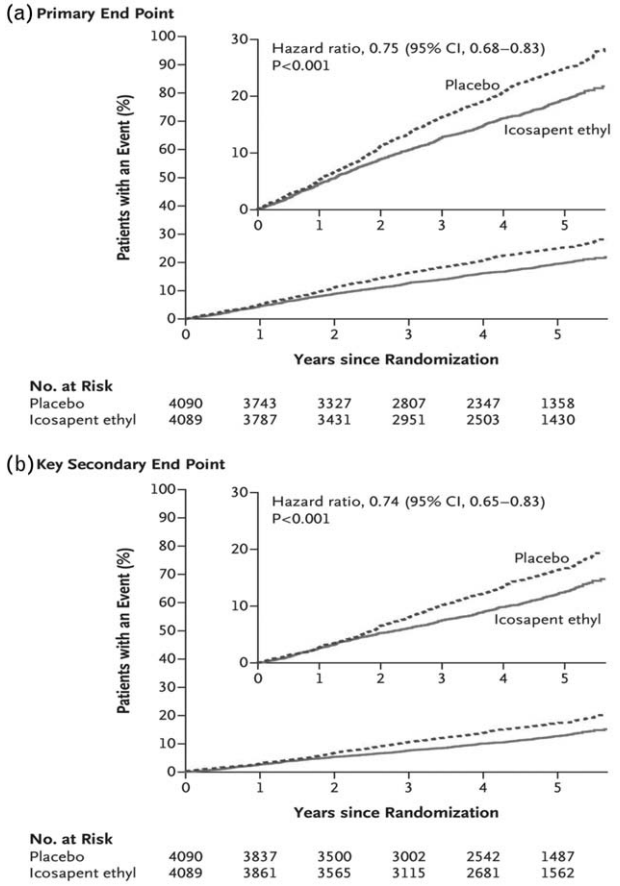

FIGURE 3 Panel (a) shows the Kaplan–Meier event curves for the primary efficacy composite end points of cardiovascular death, nonfatal myocardial infarction, nonfatal strokes, and coronary revascularization, or unstable angina in the icosapent ethyl group and the placebo group. Panal (b) shows the Kaplan–Meier event curves for the key secondary efficacy composite end point of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke in the two trial groups [55].

antihypertensive therapy, acupuncture significantly reduced SBP (−8 mmHg, $P < 0.00001$) and DBP (−4 mmHg, $P < 0.0001$) and no heterogeneity was detected. Considering the limitation of the studies, heterogeneity, and small sample size, the authors concluded their results to be inconclusive. In a more recent meta-analysis, Li *et al.* [59] compared BP-lowering effects of acupuncture vs. sham procedure in individuals with hypertension. In this study, acupuncture resulted in a significant reduction in SBP and DBP among those patients taking antihypertensive medications. In patients not taking antihypertensive medications, acupuncture failed to reduce SBP, but did reduce DBP. Minor adverse events, including pain at needle site and bleeding were reported. Based on these studies, at the most, acupuncture may accentuate the antihypertensive effect of BP-lowering agents, but certainly does not merit utility as a standalone therapy for hypertension.

YOGA

Yoga is an ancient practice that incorporates postures, breathing techniques, and meditation. Of the many proposed benefits of yoga, BP control is among the most studied. Hagins *et al.* [60] examined the BP-lowering effects of yoga in adults with hypertension. This meta-analysis included 17 studies of varying duration and yoga techniques. Yoga had a modest but significant effect on SBP (−4.17 mmHg, $P = 0.0002$) and DBP (−3.6 mmHg, $P = 0.0001$). In a subgroup analysis, yoga that involved three elements of practice (posture, meditation, and breathing) is associated with significant reduction in BP, whereas yoga interventions using two or fewer elements of yoga practice did not reduce BP. The duration of yoga practice did not seem to impact BP response. Most studies assessed gentle yoga programs and relatively short duration, which could easily be implemented into clinical practice. Since none of the included studies had methodologies with low risk of bias, additional rigorous controlled trials are warranted to further investigate the potential BP-lowering effects of yoga in the hypertensive population.

BREATHING TECHNIQUES

Slow deep breathing has long been thought to have BP-lowering effects. The mechanism behind the favorable BP effects may be related to quieting overactivity of the central nervous system by resetting thresholds for cardiopulmonary and arterial baroflex/chemoreflex receptors [61]. Regular slow and deep breathing can reduce SBP and DBP, in comparison with normal breathing [62]. There are several methods to achieve slow breathing. One device has received FDA approval as an adjunct treatment to reduce BP [63]. This system uses a belt around the thorax to monitor breathing rate, which feeds to real-time data controller box, which in turns generates musical tones into headphones during inspiration and expiration [64]. The antihypertensive effects have been evaluated in 13 clinical trials of various sizes. The weighted average reduction in office BP at 8–9 weeks compared with baseline was 13/7 vs. 9/4 mmHg ($P < 0.01$) [65]. A threshold effect on BP reduction was seen at approximately 15 min with device use. Studies that measured home BP demonstrated a reduction after about 1–2 weeks of daily use. In conclusion, device-guided breathing technique may lower BP; however, independent and larger studies are required to provide definitive evidence.

MEDITATION

Meditation has garnered attention from both the general public and medical communities for its beneficial health effects, including BP reduction. Marques [66] recently performed a RCT examining the effect of meditation on BP among individuals with established hypertension. After 8 weeks, the intervention group had statistically significant lower ambulatory BP measurement than the control group [124/77 vs. 126/80 mmHg ($P < 0.05$) and 108/65 vs. 114/69 mmHg ($P < 0.05$) for 24-h and night-time SBP, respectively, and also had lower clinically measured SBP values (130 vs. 133 mmHg; $P = 0.02$)]. At week 20, the BP response with meditation compared with control did not reach statistical significance. Despite the positive results of this study, the breadth of research examining the impact of meditation on BP shows a more varied BP response [67]. The heterogeneity in the results reflect varying study populations, designs, protocols, duration, and BP measurement

techniques. This heterogeneity greatly hinders the ability to make concrete inferences regarding the impact of meditation on BP. That being said, numerous studies have demonstrated modest BP reduction associated with meditation. Moreover, meditation is safe, easy to implement, and can be performed anywhere. In the 2013, AHA scientific statement on alternative approaches to lowering BP concluded that meditation modestly lowered BP and its use can be considered for patients with hypertension [4].

FASTING

Intermittent fasting is a form of time restricted eating (typically 16 h fasting and 8 h eating), which has gained popularity in recent years and shows promise as a possible dietary strategy for the expanding obesity epidemic. Early data suggest that intermittent fasting improves cardiovascular markers, reduces fat mass (particularly the trunk fat), and improves the fat-to-lean ratio [68]. A few studies have examined the effect of intermittent fasting on BP in overweight and obese individuals with positive results [11,69]. One recent study examined the effect of intermittent fasting on BP in individuals with untreated prehypertension or established hypertension [70]. Intermittent fasting produced a significant decrease in SBP values in terms of office BP (122.75 mmHg before intermittent fasting vs. 116.88 mmHg during intermittent fasting, $P < 0.01$). In addition, 24-h urine sodium excretion was lower in the intermittent fasting group compared with the control group (234.50 mEq/day compared with 213 mEq/day, $P = 0.04$). Some preliminary data suggest that heightened parasympathetic activity associated with intermittent fasting may be responsible for the BP-lowering effects [71]. Intermittent fasting seems to have promise as a strategy for weight loss and BP control. Further research is necessary to determine if the positive effects of intermittent fasting on BP occur independently of weight loss.

CONCLUSION

Traditional pharmacologic and lifestyle modifications in accordance with the 2017 ACC/AHA guidelines are considered the standard of care for BP management. The integration of CAM-based BP reduction strategies by the medical community has been slow. This is primarily due to low-quality evidence supporting CAM-based BP treatment strategies. To date, there are no CAM-based BP therapies that have demonstrated reduction in hard cardiovascular outcomes, like MI, cerebrovascular disease, congestive heart failure, or mortality within a hypertensive cohort. Justifiably, CAM-based BP reduction strategies are not considered first-line therapy for the management of hypertension. That being said, there does exist low-quality data that these strategies can reduce both SBP and DBP, and are generally safe, well-tolerated, and easy to implement. Since nearly half of individuals with hypertension are not at goal BP, CAM-based therapies that can reduce BP may be an attractive supplemental therapy to traditional treatment options. Although these therapies should not supplant traditional BP reduction strategies, they can be employed as a complementary tool in a multipronged approach to achieving BP control.

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Conflicts of interest

There are no conflicts of interest.

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