Beyond Medications and Diet: Alternative Approaches to Lowering Blood Pressure : A Scientific Statement From the American Heart Association

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AHA Scientific Statement

Beyond Medications and Diet: Alternative Approaches to Lowering Blood Pressure

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Abstract—Many antihypertensive medications and lifestyle changes are proven to reduce blood pressure. Over the past few decades, numerous additional modalities have been evaluated in regard to their potential blood pressure–lowering abilities. However, these nondietary, nondrug treatments, collectively called alternative approaches, have generally undergone fewer and less rigorous trials. This American Heart Association scientific statement aims to summarize the blood pressure–lowering efficacy of several alternative approaches and to provide a class of recommendation for their implementation in clinical practice based on the available level of evidence from the published literature. Among behavioral therapies, Transcendental Meditation (*Class IIB, Level of Evidence B*), other meditation techniques (*Class III, Level of Evidence C*), yoga (*Class III, Level of Evidence C*), other relaxation therapies (*Class III, Level of Evidence B*), and biofeedback approaches (*Class IIB, Level of Evidence B*) generally had modest, mixed, or no consistent evidence demonstrating their efficacy. Between the noninvasive procedures and devices evaluated, device-guided breathing (*Class IIA, Level of Evidence B*) had greater support than acupuncture (*Class III, Level of Evidence B*). Exercise-based regimens, including aerobic (*Class I, Level of Evidence A*), dynamic resistance (*Class IIA, Level of Evidence B*), and isometric handgrip (*Class IIB, Level of Evidence C*) modalities, had relatively stronger supporting evidence. It is the consensus of the writing group that it is reasonable for all individuals with blood pressure levels >120/80 mm Hg to consider trials of alternative approaches as adjuvant methods to help lower blood pressure when clinically appropriate. A suggested management algorithm is provided, along with recommendations for prioritizing the use of the individual approaches in clinical practice based on their level of evidence for blood pressure lowering, risk-to-benefit ratio, potential ancillary health benefits, and practicality in a real-world setting. Finally, recommendations for future research priorities are outlined. **(*Hypertension.* 2013;61:00-00.)**

Key Words: AHA Scientific Statement ■ blood pressure ■ cardiovascular diseases ■ complementary therapies ■ hypertension ■ prehypertension ■ preventive medicine

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Hypertension is one of the most common disorders, affecting ≈26.4% of the adult population worldwide. It ranks as the leading chronic risk factor for mortality, accounting for 13.5% of all deaths.[1,2] Moreover, its prevalence is projected to grow to affect >1.5 billion people by 2025.[1,2] Half of all strokes and ischemic heart disease events are attributable to high blood pressure (BP).[1,2] Given the monotonic relationship between cardiovascular events and BP even down to optimal levels (115/75 mm Hg), the global hypertension-related public health burden is enormous.[3]

An important component of the overall strategy to prevent the adverse health consequences of hypertension is the recommendation promulgated by formal guidelines for individuals to adopt lifestyle changes that reduce BP.[4–6] Proven approaches promoted by the guidelines include weight loss, reduced sodium intake, adoption of a Dietary Approaches to Lower Hypertension–style eating pattern, aerobic exercise for 30 minutes on most days per week, and moderation of alcohol intake.[7–10] In this regard, the American Heart Association (AHA) published a scientific statement in 2006 outlining these dietary approaches to treat and prevent hypertension.[11] These strategies were later endorsed by the American Society of Hypertension.[12] Given the high prevalence of BP levels above optimal[13] and the 90% lifetime risk for developing hypertension among middle-aged adults with normal blood pressure,[14] these dietary recommendations apply not only to individuals with hypertension but also to individuals with prehypertension and to a large portion of the general populace.

Aims and Rationale

Beyond dietary strategies, certain additional nonpharmacological treatments may have the capacity to lower BP.[9,15,16] For the purposes of this scientific statement, these therapies are called alternative approaches and are broadly classified into 3 categories: behavioral therapies, noninvasive procedures or devices, and exercise-based regimens. There are several reasons why these strategies are likely to become increasingly important and commonly used tools in the management of high BP. First, adherence to dietary strategies has often been shown to be difficult to maintain.[13,17] Some of the alternative approaches outlined in this document may in theory be more readily adopted and thus serve as practical adjuvants to help lower BP. However, it is recognized that long-term effectiveness and adherence have not been established for most of these approaches, and the degree to which they are adopted when recommended by physicians will likely vary among individuals and approaches.[18] Second, many of these alternative approaches may represent viable methods to help treat prehypertension. There is growing evidence that prehypertension not only predicts an increased risk for the development of hypertension but also confers an increased risk for cardiovascular events.[19,20] Given the paucity of evidence supporting the cost-effectiveness of pharmacological therapy,[21,22] these approaches may represent practical options for some individuals with prehypertension. Third, in accordance with guidelines, healthcare providers may offer a trial of nonpharmacological interventions (including alternative modalities) as part of the initial treatment of stage I hypertension among individuals wishing to avoid or delay drug therapy when clinically appropriate.[4] Fourth, there is an increasing prevalence of resistant hypertension.[23] Combination strategies incorporating these alternative approaches might be helpful to achieve BP control among individuals with resistant hypertension. Fifth, most of the reviewed alternative approaches pose little to no side effects and could thus represent acceptable options for individuals with multiple medication intolerances. Finally, despite numerous efforts for the nationwide promulgation of healthy lifestyles, the number of individuals with hypertension in the United States continues to grow, most recently estimated at 29% of adults.[13] Alternative approaches represent adjuvant nonpharmacological modalities to help combat this prevalent and expensive disorder.

At present, most of these benefits remain hypothetical because they have yet to be directly tested. Furthermore, many of the published studies assessing alternative approaches have been observational in nature. Even among published randomized trials, methodological weaknesses, including inadequate randomization methods and the inclusion of suboptimal control groups, small sample sizes, and brief follow-up durations (eg, 3–6 months), are common. Other prevalent limitations include selection, proficiency, compliance, and cointervention biases. The lack of inclusion of home or ambulatory BP monitoring (ABPM) outcomes in many studies is also a significant shortcoming. Finally, with few exceptions, there is a paucity of outcome trials demonstrating that these alternative approaches are capable of reducing hard cardiovascular events. On the other hand, most currently recommended nonpharmacological interventions (eg, exercise, smoking cessation) have not undergone rigorous testing among outcome trials; hence, this may be an unrealistic standard before the use of alternative approaches is recommended specifically for BP lowering, provided that they are efficacious in this regard and generally safe.

Regardless of these limitations, the major justification for this review is the plausibility that these treatments could offer substantive public health benefits provided that they indeed effectively reduce BP. BP lowering per se is acknowledged as an accepted surrogate marker that reliably predicts the cardiovascular health benefits of an intervention so long as it is not offset by other treatment-related risks.[24,25] Apart from the small risk of developing worse hypertension by delaying medical treatment as seen in a few trials, most alternative approaches pose little direct health risks. Therefore, the principal objective of this scientific statement is to provide an up-to-date assessment of the evidence supporting the BP-lowering efficacy of several alternative approaches. Although some of these treatments have been reviewed on an individual basis, our aim is to provide a comprehensive summary for healthcare providers within a single document. Although some of the therapies (eg, exercise, yoga, meditation, and acupuncture) also have the potential to provide health or psychological benefits beyond BP lowering, these outcomes are beyond the scope of this document. The second goal is to provide practical recommendations for incorporating these modalities into clinical practice on the basis of the currently available published trial evidence. Finally, suggested future research priorities are outlined.

Methods and Evidence Review

An initial online review of the English language literature was performed with PubMed that included alternative BP-lowering approaches and excluded orally active agents such as dietary changes, complementary therapies, herbs, and novel medications. The writing group then classified the approaches into 3 broad categories: behavioral therapies, including meditation techniques, yoga, biofeedback, and relaxation or stress-reduction programs; noninvasive procedures or devices, including device-guided breathing modulation and acupuncture; and exercise-based regimens, including aerobic, resistance, and isometric exercise methods.

The initial search identified a meta-analysis or comprehensive review for each topic that was published within the past 6 years. A systematic literature search limited to human studies and the English language was next performed in PubMed for publications between January 1, 2006, and October 31, 2011, for each of the above methodologies in relation to BP. These systematic searches were done to identify important studies published shortly before or after the most recent meta-analyses or review. This yielded 124, 105, and 773 publications for behavioral therapies, noninvasive procedures and devices, and exercise-based regimens, respectively. The complete list of publications is available

Table 1. Applying Classification of Recommendations and Level of Evidence

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	SIZE OF TREATMENT EFFECT			
	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	**CLASS IIa** *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	**CLASS IIb** *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	**CLASS III** *No Benefit* or **CLASS III** *Harm* Procedure/ Test / Treatment COR III: No benefit / Not Helpful / No Proven Benefit COR III: Harm / Excess Cost w/o Benefit or Harmful / Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit is not recommended is not indicated should not be performed/ administered/ other is not useful/ beneficial/ effective COR III: Harm potentially harmful causes harm associated with excess morbidity/mortality should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior MI, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

in the **online-only Data Supplement—References**. Each systematic search was conducted with the assistance of a medical librarian and used relevant keywords and medical subject headings. The details of the search strategies and terms are available in the **online-only Data Supplement—Methods and Results**. Some studies published in 2012 and/or identified from the references of other publications were added during the process of writing the scientific statement. All identified publications were then reviewed by members of the writing committee. Each treatment approach was evaluated in terms of its BP-lowering efficacy as the main outcome. The safety of each methodology and the efficacy within specific subgroups (eg, individuals with prehypertension) were also evaluated when germane information was available. The individual approaches were then assigned an official level of evidence (LOE) and class of recommendation (COR) per AHA guideline criteria based on the expert opinion of the writing group members (http://www.heart.org/HEARTORG/) (Table 1).[26] During this decision process, emphasis was given to the findings from the most recent high-quality systematic meta-analyses, which also included studies published before the start date of the systematic review. Next, identified studies published after the latest meta-analysis were individually assessed. Their findings were evaluated to assess whether they substantially added to the overall level of data supporting the efficacy of each approach. Randomized, controlled clinical trials in which outcomes were assessed in a blinded fashion were given the most weight in the decision processes.

Organization of the Writing Group

Writing group members were nominated so that the writing group could comprise healthcare providers and scientists with a breadth of expertise in the fields of clinical hypertension, cardiology, exercise physiology, cardiac rehabilitation, and dietary-lifestyle treatments for cardiovascular disease prevention and hypertension management. The members were selected by the co-chairs of the writing group and by the AHA Manuscript Oversight Committee. The Manuscript Oversight Committee also provided formal approval of the final roster and of the scientific statement outline.

Scope of the Guidelines

This scientific statement does not represent a meta-analysis of all published studies for each alternative BP-lowering modality. Rather, the focus is to perform a review of the evidence supporting the BP-lowering efficacy of each treatment and to provide an LOE and a COR for each approach.[26] A secondary goal is to provide expert opinion–based recommendations for the implementation of these approaches within clinical practice for the management of high BP. A systemic review of the numerous additional alternative approaches, including dietary treatments (eg, herbs, nutraceuticals), is beyond the scope of this document. Procedures that are currently experimental and treatments that apply only to select subgroups of individuals underwent an abbreviated nonsystematic review.

Behavioral Therapies

Several alternative approaches can be categorized within the framework of behavioral therapies. Although these methods vary considerably, the techniques included in this scientific statement have been studied in terms of their BP-lowering potential either as a primary trial outcome or as an ancillary health benefit. An intrinsic difficulty in interpreting the results of behavioral interventions is that many represent a combination of several individual approaches (eg, relaxation plus meditation and/or deep breathing). Thus, the separation of these techniques into individual methods is somewhat artificial and must be recognized as a limitation. We have, whenever possible, included techniques that were the predominant intervention and acknowledged whether they included additional methods when relevant. Another limitation of some of the randomized studies is the difficulty in assigning an appropriate control intervention.

Meditation Techniques

Meditation has been part of human societies in various forms for thousands of years. The optimal manner to categorize the myriad techniques is open to opinion. It should be emphasized that their origins typically relate to endeavors to improve awareness or consciousness and have little to do with the treatment of hypertension. In the limited context of this review, we have divided practices into focused attention (ie, mantra and training awareness); Transcendental Meditation (TM), a technique to transcend thought and to experience pure awareness, typically by employing specific mantras; and contemplative forms (eg, Zen and mindfulness), including the Mindfulness-Based Stress Reduction (MBSR) program.[27–30] Further details are found in the **online-only Data Supplement—Methods and Results**.

Meta-Analyses or Reviews

The Healthcare Research and Quality report published an evidence-based document on meditation practices for health in 2007.[31] The University of Alberta Evidence-Based Practice Center was commissioned to prepare the report. It was requested and funded by the National Center for Complementary and Alternative Medicine and included published studies through 2005. For hypertension, 5 trials of TM, 2 trials of Zen meditation, and 2 other trials of meditation without a clear description (which were not included in the meta-analysis) were reviewed. Only 2 trials (both of TM) were considered to be of high methodological quality. The studies of TM had sample sizes ranging from 37 to 106 and were medium- to long-term interventions (≥3 months). TM was found to be superior to progressive muscle relaxation with respect to reductions in systolic (−4.30 mm Hg; 95% confidence interval [CI], −6.02 to −0.57) and diastolic (−3.11 mm Hg; 95% CI, −5.00 to −1.22) BP but not to health education (systolic BP, −1.10 mm Hg; 95% CI, −5.24 to 3.04; diastolic BP, −0.58 mm Hg; 95% CI, −4.22 to 3.06). Compared with repeated measurement of BP (“BP checks”), Zen meditation was found to produce reductions in diastolic BP (−6.08 mm Hg; 95% CI, −11.68 to −0.48) but not systolic BP (−3.67 mm Hg; 95% CI, −9.04 to 1.70). For healthy individuals, 3 studies of TM were found for inclusion in a meta-analysis of TM compared

with no treatment. TM was not associated with greater systolic (0.93 mm Hg; 95% CI, −9.53 to 11.39) or diastolic (−1.63 mm Hg; 95% CI, −8.01 to 4.75) BP reductions.

Since the Healthcare Research and Quality report, 2 additional meta-analyses evaluating the effects of TM on BP have been published.[32,33] They criticized the Healthcare Research and Quality report on several methodological grounds. Many of the studies included in both meta-analyses overlapped. In addition, numerous individual studies were ultimately not included in the final statistical analyses because of poor quality. The meta-analysis published in 2007 comparing TM with attention control included 6 randomized, controlled trials of at least 8 weeks' duration that were thought to be well designed with a total of 449 individuals. TM was associated with significant reductions in both systolic (−5 mm Hg; 95% CI, −7.6 to 2.3) and diastolic (−2.8 mm Hg; 95% CI, −5.0 to −0.5) BP.[33] A separate meta-analysis published in 2008 included 9 randomized, controlled trials suitable for analysis (367 individuals in active and 344 in control groups). It compared TM with health education (7 studies), relaxation (1 study), or no treatment (1 study).[32] The studies varied in duration from 8 to 52 weeks (median, 15 weeks) and included individuals with normal blood pressure (n=3), with prehypertension (n=2), and with overt hypertension (n=4). For all studies, the outcomes were clinic-measured BP averages. TM was associated with significant reductions in both systolic (−4.7 mm Hg; 95% CI, −1.9 to −7.4) and diastolic (−3.2 mm Hg; 95% CI, −1.3 to −5.4) BP compared with control arms. Similar reductions were reported for individuals with hypertension and individuals with normal blood pressure.

Recent Trials

A recent trial of TM randomized 298 university students with normal blood pressure to TM or wait-list control. The trial was a single-blind study; the primary outcome was clinic BP. Students randomized to TM did not have a reduction in BP unless they were deemed to be at high risk for hypertension (ie, body mass index >25 kg/m^2, BP >130/85 mm Hg, and/or a self-reported family history of hypertension).[34] The effect of TM versus health education was also recently assessed in a randomized, controlled trial for the secondary prevention of cardiovascular disease among 201 blacks.[35] During an average follow-up of 5.4 years, the primary end point (composite of all-cause mortality, myocardial infarctions, or stroke) was significantly reduced by 48% (hazard ratio, 0.52; 95% CI, 0.29–0.92) in the TM group. Compared with the control group, systolic BP was 4.9 mm Hg lower (95% CI, −8.3 to −1.5) at the end of the trial among those randomized to TM. However, this net difference was attributable to an increase in systolic BP in the control group (4.9 mm Hg) rather than a significant reduction induced by TM treatment (0.02 mm Hg). In this regard, TM may have played a role in preventing aging-related BP progression over half a decade. More long-term follow-up research is required.

Recent studies have also evaluated the effectiveness of contemplative forms of meditation, including mindfulness meditation and MBSR.[36–42] Two trials were conducted in children and randomized participants in groups (eg, by class). One randomized trial compared breathing awareness meditation with life skills training and health education in 166 black ninth grade students with elevated resting systolic BPs.[40] Interventions were conducted by teachers in health education classrooms for 1 semester (ie, 3 months). Breathing awareness meditation produced a greater decrease in 24-hour systolic BP (3.1±1.0 mm Hg) compared with the other treatments and a 2.0±0.8-mm Hg decrease in diastolic BP compared with life skills training. The other trial compared 3 months of daily mindfulness meditation with health education in 73 seventh grade students with normal blood pressure.[36] Meditation produced a larger decrease in resting systolic BP (−2.7 mm Hg) compared with the increase (1.1 mm Hg) observed in the health education condition.

Three small, randomized trials evaluated the effects of slightly different forms of meditation, 2 in individuals with normal blood pressure that did not demonstrate any effects on BP[39,41] and 1 in individuals treated for hypertension.[42] The first 2 trials involved 4 weeks of body-scan meditation or mindfulness meditation in university students with normal blood pressure and were compared with no intervention or guided imagery, respectively.[43] Both trials did not demonstrate differences in BP compared with control interventions. The trial in nonmedicated individuals with hypertension involved randomization to 8 weeks of meditation or no intervention.[42] Reductions in resting clinic systolic BP (median, −15 mm Hg) and in ambulatory systolic and diastolic BPs were reported in the meditation group. Finally, 2 nonrandomized studies evaluated the effects of completing an 8-week MBSR program on BP in individuals with cancer. The first was a preintervention-versus-postintervention comparison of BP in 59 individuals with cancer at 6 time points (for up to 12 months).[44] A small decrease in systolic BP (2.1 mm Hg) was observed from pretesting to postintervention assessments. The second study was a wait-list controlled study comparing the MBSR program and no treatment in 76 women with cancer.[37] MBSR was not associated with reduced BP by the end of the 8-week intervention, although subgroup analyses suggested that MBSR may have reduced systolic BP in women who initially had higher levels.

Finally, the results of a well-designed trial randomizing 101 untreated adults with stage I hypertension to an MBSR program versus a wait-list control were recently presented.[45] After 12 weeks, the BP differences between groups measured by ambulatory monitoring were not different (0.0±7.2/0.4±4.7 mm Hg). The investigators noted that prior studies reporting positive findings were conducted among individuals treated for hypertension and that the benefits related to an MBSR intervention may have been derived from superior medication adherence. Nonetheless, these important findings do not support a direct BP-lowering effect of an MBSR program over a 3-month time period.

Mechanisms of BP Lowering

The mechanism whereby meditation techniques lower BP when it occurs remains unclear. It has been suggested that the mechanisms may lead to reductions in stress and physiological arousal, thereby producing favorable effects on the autonomic nervous system balance.[32,33] Further studies are needed to clarify the importance of this and other possible biological pathways.

Summary and Clinical Recommendations

The overall evidence supports that TM modestly lowers BP. It is not certain whether it is truly superior to other meditation techniques in terms of BP lowering because there are few head-to-head studies. As a result of the paucity of data, we are unable to recommend a specific method of practice when TM is used for the treatment of high BP. However, TM (or meditation techniques in general) does not appear to pose significant health risks.[32] Additional and higher-quality studies are required to provide conclusions on the BP-lowering efficacy of meditation forms other than TM.

The writing group conferred to TM a *Class IIB, Level of Evidence B* recommendation in regard to BP-lowering efficacy. TM may be considered in clinical practice to lower BP. Because of many negative studies or mixed results and a paucity of available trials, all other meditation techniques (including MBSR) received a *Class III, no benefit, Level of Evidence C* recommendation Thus, other meditation techniques are not recommended in clinical practice to lower BP at this time.

Biofeedback Techniques

Biofeedback for the management of hypertension involves the use of nonpharmacological methodologies that provide information feedback to the individual associated with the lowering of BP.[46] Techniques that may be used include cognitive behavioral therapy, relaxation therapy, guided imagery, and psychological education. The methods of biofeedback include direct BP measurement and indirect indicators such as thermal biofeedback, galvanic skin response, heart rate. and electromyographic activity. Individuals receive feedback on parameters through the use of 1 of a variety of different methodologies. When the end point (BP in these studies) reaches a prespecified level, the individual receives a feedback signal to identify thoughts and activities at that time. The individual then repeats the thoughts and activity sequences associated with this lower BP in an effort to capture the benefit associated with that scenario. Numerous clinical trials have been implemented to test the effects of biofeedback on BP reduction.[47] Biofeedback procedures have also been used in conjunction with other stress reduction techniques to have larger effects.[48]

Meta-Analyses or Reviews

Several meta-analyses and reviews of biofeedback therapy were published between 2003 and 2010.[33,47,49] These analyses acknowledged the shortcomings of biofeedback investigations in hypertension (short duration, small sample sizes, difficulties with blinding, and significant heterogeneity when trial data were combined). In addition, a number of the meta-analyses combined multiple complementary medicine techniques in their analyses, thus rendering the effects related specifically to biofeedback alone difficult to assess. The use of different methodologies to assess BP may have also affected the ability to discern small changes. Both of the most recent meta-analyses did not report statistically significant overall BP reductions with biofeedback.[33,47] For example, in a 2007 meta-analysis, use of biofeedback techniques alone produced small nonsignificant decreases in systolic (−0.8 mm Hg; 95% CI, −4 to 2.6) and diastolic (−2.0 mm Hg; 95% CI, −5.1 to 1.2) BPs among 6 trials including 141 individuals in total.[33]

As further testament to the difficulty of performing overviews of the antihypertensive efficacy of biofeedback, 2 systematic reviews assessing biofeedback in hypertension reached different conclusions. A 2003 review identified biofeedback as more effective than nonintervention (sham or nonspecific behavioral intervention) when combined with relaxation.[49] This review was limited in multiple respects, including a pooling of results that was weak in justification. On the other hand, a systematic review done in 2010 that included strict study inclusion assessment found no evidence for the effectiveness of biofeedback in regard to hypertension control compared with placebo, no intervention, pharmacotherapy, and/or behavioral therapy.[47] As with most interventions, there has been a wide range of reported individual patient- and trial-specific BP responses. The spread of systolic BP reductions among trials using biofeedback in the literature spans values ranging from none to ≈15 mm Hg.[50]

Recent Trials

In a small randomized trial using ABPM, a significant −8/−5–mm Hg reduction in individuals randomized to biofeedback compared with controls was reported.[51] This difference, however, was not evident with office BP measurements. As outlined in the earlier meta-analysis by the same first author,[50] treatment effects of biofeedback may be dependent on the starting BP values, being larger in those with untreated hypertension (>140/>90 mm Hg) with smaller reductions noted among individuals with normal blood pressure or individuals taking antihypertensive medications.

In a recently published trial, 65 individuals with hypertension were randomized to biofeedback training combined with behavioral relaxation (behavioral neurocardiac training) versus active control consisting of autogenic training (repetitive visualizations to induce a state of relaxation) over 2 months.[52] Training in behavioral neurocardiac training and in the control was supplemented by 20-minute audiotaped exercises for daily home practice. Behavioral neurocardiac training reduced daytime and 24-hour systolic BP levels (−2.4±0.9 mm Hg, P=0.009, and −2.1±0.9 mm Hg, P=0.03, respectively). No effects were observed in individuals in the control group. Behavioral neurocardiac training also increased RR high-frequency power (0.15 to 0.40 Hz; P=0.01) and RR interval (P<0.001) during cognitive tasks. Among individuals in the control group, high-frequency power was unchanged (P=0.29) and RR interval decreased (P=0.03). Neither intervention altered spontaneous baroreflex sensitivity (P>0.10).

Patient factors responsible for achieving a ≥5-mm Hg systolic BP reduction through biofeedback-assisted relaxation have also been assessed. Being medically untreated and having the lowest finger temperatures, the smallest standard deviations of BP during ABPM, and the lowest scores on a psychological test were the best predictors of BP responsiveness.[53]

Mechanisms of BP Lowering

The mechanisms responsible for the BP lowering induced by biofeedback when it occurs are incompletely described. There is some evidence that favorable alterations in autonomic nervous system balance may be involved.[47,52] Additional studies

are required to determine the precise pathways responsible when biofeedback produces a reduction in BP.

Summary and Clinical Recommendations

Although meta-analyses results are mixed, some recent trials have shown that certain biofeedback techniques can reduce BP.[51,52] It is plausible that some techniques may be more effective than others[52]; however, a paucity of data precludes making recommendations for implementing a specific methodology to treat high BP in clinical practice. On the other hand, no significant health risks were reported among the trials.[47,52]

The writing group conferred to biofeedback techniques in general a *Class IIB, Level of Evidence B* recommendation in regard to BP-lowering efficacy. Biofeedback may be considered in clinical practice to lower BP.

Yoga

The term yoga (Sanskrit meaning union) has many connotations. It originated in ancient India as primarily a word to describe a contemplative state with the aim of cessation of mental activity and attainment of a state of superior consciousness. Its many complexities and various forms are briefly outlined in the online-only Data Supplement—Methods and Results.

Meta-Analyses or Reviews

As far as we are aware, no formal meta-analysis of the effects of yoga on BP has been performed. Two literature reviews have been published since 2007.[54,55] Most studies were small and executed outside North America or Europe. The majority were uncontrolled case series or small cohort studies with significant methodological limitations. The published randomized trials often suffered from small sample sizes, inadequate control groups, or a lack of control for many other factors.[38,56–59] The effect of yoga intervention per se was commonly difficult to assess because concomitant lifestyle changes were frequently undertaken. Finally, BP was rarely the primary outcome of interest, with ABPM used in only a few studies.

A recent 2012 review qualitatively discussed studies published between 2006 and 2011.[55] The authors stated that BP was lowered by yoga in 8 of the 9 studies evaluated. An earlier review in 2007 discussed the effects of yoga on multiple cardiovascular risk factors in studies published from 1980 to 2007.[54] A total of 32 articles were reviewed. Reductions in BP were noted in 25 studies; however, it was not clear whether BP was unchanged or not measured in the other 7 studies. As previously outlined, there were significant methodological and reporting limitations in many of the individual studies.

Recent Trials

There have been a limited number of reports published in the past few years attesting to the effects of various yoga programs on BP. Two small randomized studies of hatha yoga–type practices evaluated BP as an outcome since 2007.[60,61] A third small trial assessed the impact of a variation of pranayama on a background of hatha yoga practice. In a randomized, controlled clinical trial, yoga-naïve adults with stage I hypertension were randomized to 12 weeks of Iyengar yoga or control arms (enhanced usual care emphasizing diet).[60] In total, 26 and 31 individuals in the yoga and control arms, respectively, completed the study. In the control group, 24-hour systolic, diastolic, and mean arterial pressure BPs decreased significantly by 5, 3, and 3 mm Hg, respectively, from baseline to 6 weeks ($P<0.05$ versus baseline) and 4, 2, and 2 mm Hg at 12 weeks (P=NS versus baseline). In the yoga group, 24-hour systolic, diastolic, and mean arterial BPs were unchanged compared with baseline at 6 weeks but were reduced by 6, 5, and 5 mm Hg, respectively, at 12 weeks ($P=0.05$ versus baseline). No differences were observed in catecholamine or cortisol metabolism. In this small study, although there were no differences between the 2 interventions, the reductions seen at 12 weeks with yoga were comparable to what is typically observed with other lifestyle changes.

In the second randomized trial, HIV-infected adults (n=60) with mild to moderate cardiovascular risk were assigned to 20 weeks of supervised Ashtanga Vinyasa yoga or standard of care treatment.[61] Baseline and week 20 measures included BP and 2-hour oral glucose tolerance testing with insulin monitoring, body composition, fasting serum lipid/lipoprotein profile, and quality-of-life measures. Resting systolic and diastolic BP levels improved more ($P=0.04$) in the yoga group (−5±2 and −3±1 mm Hg, respectively) than in the standard of care group (1±2 and 2±2 mm Hg, respectively) without improvement in other measures noted.

In a trial performed in Brazil, 76 elderly individuals were randomized to a variation of yogic pranayama breathing called Bhastrika on a background of hatha yoga.[62] Pulmonary function, heart rate, and BP variability for spontaneous baroreflex determination were measured at baseline and after 4 months. In the yoga group, there were significant decreases in the low-frequency component heart rate variability (a marker of cardiac sympathetic modulation), along with the low-frequency/high-frequency ratio, a marker of sympathetic-vagal balance ($P<0.001$). Spontaneous baroreflex sensitivity did not change and quality of life only marginally increased in the yoga group.

Mechanisms of BP Lowering

Few studies have evaluated the possible mechanisms whereby yoga might alter BP. The limited evidence suggests that it might be capable of favorably altering autonomic balance.[62] Whether additional pathways are involved requires future investigation.

Summary and Clinical Recommendations

There are limited data from high-quality, randomized, controlled trials pertaining to the potential BP-lowering efficacy of yoga in and of itself. Additional larger and higher-quality trials are needed. Therefore, a specific technique cannot be recommended. On the other hand, beyond the potential for musculoskeletal injuries, there are few ostensible cardiovascular health risks posed by yoga practice, and no adverse events have been reported in the few completed trials.

Because of the scarcity of reliable study results and the mixed findings from randomized, controlled studies, no firm conclusions can be drawn; thus, the writing group ascribed to yoga a *Class III, no benefit, Level of Evidence C* recommendation for BP-lowering efficacy. Yoga techniques are not recommended in clinical practice to lower BP at this time.

Other Relaxation Techniques

Relaxation and stress-reduction programs can be heterogeneous in nature and often comprise a multitude of approaches used in conjunction. This makes a uniform assessment of the treatment-associated BP-lowering responses difficult. There may also be overlap in the methods used to elicit a relaxation response with the approaches previously reviewed (eg, meditation).

Meta-Analyses or Reviews

Whether relaxation and stress reduction reduce BP has been studied for >40 years. In 1988, the Hypertension Intervention Pooling Project integrated data from 12 randomized, controlled trials and concluded that relaxation provided a small treatment effect for diastolic but not systolic BP among individuals with hypertension not taking medication.[63] After this report, a review performed in 1991 concluded that the effects of relaxation seemed to depend on the study design.[64] Individuals with higher initial BP levels appeared to benefit more. Studies incorporating multiple pretreatment baseline BP values among individuals demonstrated a smaller effect, suggesting the possibility of regression to the mean and a habituation effect as individuals acclimate to repeated BP measurements.

In the case of stress management treatments for hypertension, 2 early meta-analyses reported varying effects. A review performed in 1993 reported that single-component therapies (eg, relaxation alone) did not provide greater BP reductions than appropriate controls or self-monitoring of BP.[65] However, multicomponent stress management treatments were associated with reductions of 13.5 and 3.4 mm Hg for systolic and diastolic BPs, respectively, compared with sham treatments. Another review published in 1994 also reported that multicomponent stress management therapies were more effective in reducing BP than single-component relaxation-based therapies.[66]

The most recent meta-analysis is the Cochrane Review published in 2008. It evaluated the results from 25 trials including several different types of "relaxation therapies" that were used for ≥8 weeks' duration among 1198 individuals not taking antihypertensive medications with BP levels ≥140/85 mm Hg.[67] Techniques evaluated included cognitive or behavior therapy, progressive muscle relaxation, and autogenic training. Some control groups used sham therapy; other trials compared active treatment with no intervention alone. Given these limitations and after the exclusion of 1 poor trial, relaxation treatments as a heterogeneous group produced small decreases in systolic (−4.6 mm Hg; 95% CI, −6.9 to −2.2) and diastolic (−2.9 mm Hg; 95% CI, −4.5 to −1.3) BPs. However, results from sensitivity analyses and the findings limited to specific subgroups were less compelling. For example, results from trials with blinded outcomes (−3.2 mm Hg; 95% CI, −7.7 to 1.4) or those that included sham control groups (−3.5 mm Hg; 95% CI, −7.1 to 0.2) were not statistically significant.

In terms of specific techniques, this meta-analysis also demonstrated modest but significant BP-lowering effects of cognitive behavioral therapy (11 trials) and progressive muscle relaxation (16 trials) but not autogenic training (6 trials). Relaxation studies with cognitive behavior therapy lowered systolic (−6.3 mm Hg; 95% CI, −11.7 to −0.8) and diastolic (−4.1 mm Hg; 95% CI, −8.0 to −1.1) BP. Relaxation trials using progressive muscle relaxation lowered systolic (−4.8 mm Hg; 95% CI, −7.3 to −2.4) and diastolic (−2.8 mm Hg; 95% CI, −4.8 to −0.9) BPs. However, when reviewing their overall findings, the authors felt that the evidence supporting the BP-lowering efficacy of relaxation therapies was weak because of the poor quality of most trials. In addition, the BP-lowering effects were not significant among all the methods when a sham control group was included. Relaxation therapies were also associated with a small risk for worsening or uncontrolled hypertension resulting from delaying medical treatment in the trials.[67] In light of these limitations, it was suggested that further higher-quality studies are required to conclude that relaxation techniques effectively and safely lower BP. In agreement with this conclusion, a previous meta-analysis reported nonsignificant decreases in BP by relaxation therapy using progressive muscle relaxation (−1.9/−1.4 mm Hg; 2 trials) and stress management (−2.3/−1.3 mm Hg; 5 trials) programs.[32]

Recent Trials

A recent stress management trial compared the effects of 12 sessions of listening to 12 minutes of an audio relaxation program or music (Mozart) among 41 older adults.[68] The reduction in systolic BP was greater in the audio relaxation program. However, the BP levels at 1 and 3 months were not significantly lower than the initial measurements. In another randomized trial, relaxation response training was compared with lifestyle modification in 122 elderly adults with isolated systolic hypertension.[69] After 8 weeks, the degree of systolic BP reduction was not significantly different between groups. However, the authors noted that the relaxation group was significantly more likely to successfully eliminate the use of a BP-lowering medication while maintaining similar BP control. Another recent trial failed to demonstrate the effectiveness of individualized behavioral psychotherapy or self-help psychotherapy for BP lowering measured by ABPM after 12 weeks.[70]

Mechanisms of BP Lowering

It has been speculated that relaxation techniques may favorably alter autonomic nervous system balance and/or the hypothalamic-pituitary-adrenal axis.[67] The precise pathways responsible when relaxation therapies produce a decrease in BP require clarification.

Summary and Clinical Recommendations

Given the variety of methods used in the relaxation trials, the heterogeneity of results, the overall poor quality of most studies, and the frequent lack of appropriate control groups, it is difficult to conclude whether specific techniques or relaxation therapies as a general group lower BP. The meta-analysis findings also suggest that there is a small risk for worsening hypertension while medical treatment is delayed.[67] However, there was no reported direct cardiovascular harm imparted by using relaxation treatments per se.

As a result of the large number of trials with mixed results and numerous limitations, the writing group ascribed to relaxation techniques (as a group) a *Class III, no benefit, Level*

of Evidence B recommendation for BP-lowering efficacy. Relaxation techniques are not recommended in clinical practice to reduce BP at this time.

Noninvasive Procedures and Devices

Acupuncture

Acupuncture has been postulated to lower BP for a number of decades. A 1996 report from the World Health Organization indicated that acupuncture is a suitable treatment for early hypertension.[71] There are 2 basic forms of acupuncture, known as manual acupuncture and electroacupuncture.

Meta-Analyses or Reviews

To date, 2 systematic reviews and meta-analyses have evaluated the BP-lowering responses imparted by acupuncture. The first review, published in 2009, evaluated the results of 11 randomized, controlled trials[72]; the second more recent review, published in 2010, included the results from 20 randomized, controlled trials.[73]

In the first meta-analysis,[72] 3 sham-controlled trials were pooled. The systolic BP reduction was not significant (−5 mm Hg; 95% CI, −12 to 1), whereas the decrease in diastolic BP was marginal (−3 mm Hg; 95% CI, −6 to 0). However, significant heterogeneity among the studies was noted. In the second meta-analysis,[73] the overall findings suggested modest BP lowering for both systolic (−4.23 mm Hg; 95% CI, −6.47 to −1.99) and diastolic (−2.53 mm Hg; 95% CI, −3.99 to −1.08) BPs. Similarly, heterogeneity among the studies was found. BP was significantly lowered in the 2 high-quality studies compared with sham controls among individuals taking BP medications. Nevertheless, the authors of both meta-analyses summarized that their overall findings were inconclusive in terms of the benefit of acupuncture for BP lowering among individuals with hypertension. It is important to note the important limitations of the available studies, including methodological and design heterogeneity, small sample sizes, inconsistent inclusion of effect modulators, and differences in BP-related end points.

Major Trials Included in the Meta-Analyses

There are 3 individual studies of reasonable quality determined by an Oxford scale of ≥4 (maximum, 5) or a score of ≥6 on the 11-point scale developed by the Cochrane Review Group. The first study, conducted in Germany, was a single-blind, randomized, controlled trial that compared the effect of a 6-week traditional Chinese acupuncture (n=83) and sham acupuncture (identical needling at nonacupoints; n=77) on 24-hour ambulatory BP reduction among individuals treated for hypertension.[74] After the 22-session treatment, individuals in the active arm experienced significantly lower mean 24-hour ambulatory BP compared with those in the sham acupuncture arm (difference, 6.4 mm Hg [95% CI, 3.5–9.2] and 3.7 mm Hg [95% CI, 1.6–5.8] in 24-hour systolic and diastolic BPs, respectively); however, the effect disappeared and BP returned to pretreatment levels 3 and 6 months after cessation of acupuncture therapy. The second high-quality study, conducted in South Korea, was a double-blind, randomized, controlled trial that compared the effect of acupuncture as an add-on to antihypertensive medication or lifestyle changes compared with sham acupuncture (nonpenetrating needles at the same acupoints) among 41 individuals with hypertension and prehypertension.[75] Thirty individuals with hypertension being treated with antihypertensive medication completed the trial with a significant BP reduction noted with the active acupuncture after 8 weeks of intervention from 136.8/83.7 to 122.1/76.8 mm Hg. Finally, the third and largest study, the Stop Hypertension With the Acupuncture Research Program (SHARP), was conducted in the United States and included 192 individuals with untreated hypertension.[76] Study participants were randomly assigned to 1 of 3 treatment groups: traditional Chinese acupuncture (standardized), acupuncture at preselected points (individualized), or invasive sham acupuncture. The primary outcome of BP reduction from baseline to 10 weeks was not significantly different between the active arms (standardized and individualized treatment) and the sham acupuncture arm.

Mechanisms of BP Lowering

In the manual form of acupuncture, the mechanism of effect appears to be through sensory mechanoreceptor and nociceptor stimulation induced by connective tissues being wound around the needle and activated by mechanotransduction.[77] In the case of electroacupuncture, the effects appear to additionally involve the stimulation of peripheral nerve fibers, including vagal afferents, that in turn activate central opioid (and other) receptors or anti-inflammatory reflex pathways.[78] Reflex increases in sympathetic activity may also be reduced by electroacupuncture. The role of mechanoreceptor stimulation in the BP reductions in animal models is supported by the ability to attenuate this effect by gadolinium, which blocks stretch-activated channels.[79] Both forms of acupuncture have similar central nervous system effects, although electroacupuncture tends to have a greater intensity of effect as determined by functional magnetic resonance imaging studies in humans.[80] In a study of 50 untreated individuals with hypertension, manual acupuncture (which reduced BP in that study) lowered plasma renin activity from 1.7 to 1.1 $ng \cdot mL^{-1} \cdot h^{-1}$ over a 30-minute period with no change in vasopressin or cortisol concentrations.[81] An extensive review of the BP-reducing effects of electroacupuncture indicates predominantly sympathetic nervous system attenuation involving alterations in glutamate, acetylcholine, nociceptin, opioid, GABA, serotonin, and endocannibinoid neurotransmitter modulation.[82]

Summary and Clinical Recommendations

Although several studies of acupuncture have demonstrated positive effects on BP among individuals with hypertension and prehypertension, the quality of the studies is limited, so at present definite conclusions cannot be reached. It is also important to note that most studies were completed in Asian countries where acupuncture is readily available from qualified and trained medical professionals. Such training is extensive, time-consuming, and expensive, and a substantial modification in medical education and training would be required to make acupuncture accessible and available for the management of hypertension in many regions of the world. In addition to logistical difficulties in the real-world setting, meta-analyses have reported a small risk of developing uncontrolled hypertension while deferring active medical treatment and

the rare potential for minor adverse events, including pain and bleeding at needle sites.[72] Given the paucity of data, no specific acupuncture technique can be recommended over another at this time.

Because of the overall mixed study and meta-analyses results coupled with the negative findings from recent large, randomized trials, the writing group ascribed to acupuncture a *Class III, no benefit, Level of Evidence B* recommendation for BP-lowering efficacy. Acupuncture is not recommended in clinical practice to reduce BP at this time.

Device-Guided Slow Breathing

Slow deep breathing, as practiced by meditation, yoga, and several relaxation techniques, has long been thought capable of favorably affecting BP.[83–86] A short period of deep breathing (6 breaths in 30 seconds) has been shown to reduce systolic BP by 3.4 to 3.9 mm Hg within minutes in a clinic setting compared with quiet rest.[87] Beyond the short term, it has been postulated that using deep-breathing techniques over weeks to months may additionally yield long-term reductions in BP.[83,85,86]

Several methods to help achieve slow breathing have been promoted. One device has received US Food and Drug Administration approval for over-the-counter distribution "for use in stress reduction and adjunctive treatment to reduce blood pressure" (http://www.resperate.com).[88] This interactive system uses a belt around the thorax to monitor breathing rate, which feeds real-time data into a small battery-operated controller box, which in turn generates musical tones into headphones, corresponding to inspiration and expiration. Studies support that most people find it easy to use the device and experience a prompt and effortless reduction in respiratory rate as they match their breathing pattern to the musical notes.[89]

Meta-analysis, Reviews, and Recent Trials for BP Lowering

The BP-lowering effects associated with this specific Food and Drug Administration–approved device-guided slow breathing device have been evaluated in 13 clinical trials of various sizes (total number of individuals ranged from 11 to 149) and quality, sometimes compared against a control intervention (3 none, 1 usual care, 3 relaxing music, 3 home BP monitoring, or a combination thereof), typically for 8 or 9 weeks. The most appropriate control intervention is controversial, as are many issues related to study design and statistical power.[90] The pooled study population consists of 608 individuals, 55% men, average age of 57 years, 77% medicated, with an initial office BP of 150/89 mm Hg (9% with BP <140/90 mm Hg and 23% with BP ≥160/100 mm Hg). Twelve studies have now been published in peer-reviewed journals[90–101]; 2 are still in abstract form.[102,103] With 3 exceptions,[90,95,101] the trials were funded by the manufacturer and reported significant BP-lowering results (at least in per-protocol analyses). All of the trials that were independent of the manufacturer found lower office BP levels in those who used the device compared with baseline. However, no significant differences were seen across randomized groups using either 24-hour ABPM in a 4-week study of 40 individuals with prehypertension or stage 1 hypertension[90] or office BP values in 30 individuals with hypertension and diabetes mellitus[95] or 30 individuals with hypertension.[90]

In a meta-analysis of all 13 available studies performed for the purposes of this scientific statement, the weighted average reduction in office BP at 8 to 9 weeks compared with baseline with the use of the device was 13/7 versus 9/4 mm Hg for control interventions (10 studies; both $P<0.01$). Hence, the net reduction in BP induced by device-guided breathing is on the order of 4/3 mm Hg, accounting for the placebo effect in the control groups. Subgroup analyses of these overall results are confounded by small numbers of observations, cross-trial heterogeneity, and lack of patient-specific data. Nonetheless, the existing data suggest that the BP-lowering effect was independent of age, sex, and antihypertensive medication status. Both in the aggregated data and in the largest study,[92] a graded relationship was noted between the total time spent in slow breathing during the exercise and the BP-lowering effect. A threshold effect on BP lowering was seen at ≈15 minutes of use of the device (or ≈6–7 minutes of actual slow breathing) daily, consistent with the manufacturer's recommendations. Studies that measured home BP in those who use the device showed that home BP levels began to decrease after ≈1 to 2 weeks of daily use.[102] Typical of all treatments, a larger BP-lowering effect was seen among those with higher initial BP values.

A separate meta-analysis published in 2012 evaluated the BP-lowering efficacy of the device in 8 trials.[104] Overall, device use significantly lowered clinic-measured systolic (−3.67; 95% CI, −5.99 to −1.39) and diastolic (−2.51; 95% CI, −4.15 to 0.87) BPs among the 494 adults included in the analyses. Home BP levels were also significantly lowered when the results from 4 trials were pooled. The authors of this study were concerned about the potential for bias in the trials sponsored by the device manufacturer. Among the 3 remaining trials, BP was nonsignificantly lowered. The authors concluded that there is evidence that use of this device-guided breathing technique may lower BP; however, independent and larger studies are required to provide definitive evidence.

Mechanism of BP Lowering

The mechanism underlying the BP-lowering effect is complicated.[88,89,102] One hypothesis holds that autonomic imbalance plays a major role in the origin of hypertension.[103,105,106] Relative overactivity of the sympathetic nervous system eventually desensitizes cardiopulmonary and arterial baroreflex/chemoreflex receptors, leading to a resetting of threshold BP values at which regulatory signals are triggered.[107] Paced breathing with prolonged breath cycles may favorably alter (ie, reduce) chemoreceptor sensitivity, thereby decreasing arterial baroreceptor inertia and sympathetic outflow.[108] Another possible mechanism involves the fact that augmentation of tidal volume activates the Hering-Breuer reflex mediated by pulmonary stretch receptors.[109] This reduces chemoreflex sensitivity, in turn upregulating baroreflex receptor sensitivity and thereby decreasing arterial BP. It has also been suggested that paced slow breathing entrains central nervous system nuclei in which respiratory and cardiovascular centers cross-talk, thus favorably altering rhythmic sympathetic outflow to the vasculature. Small mechanistic studies suggest that the reduction in BP occurs mainly via a reduction in systemic

vascular resistance and total arterial compliance.[88,89,110,111] However, the overall biological mechanisms and the precise or integrated neural pathways involved in lowering BP by slow deep breathing remain to be fully elucidated.

Summary and Clinical Recommendations

The overall evidence from clinical trials and meta-analyses suggests that device-guided slow breathing can significantly lower BP. There are no known contraindications to the use of the device, and no adverse effects have been noted.[104] Unfortunately, the device currently costs in excess of $200 in the United States; however, it has recently been included on the British National Health Service's Drug Tariff (Part IX), which makes its cost reimbursable if prescribed by a physician. Specific recommendations for use are outlined elsewhere[110] and by the manufacturer (http://www.resperate.com). Another limitation is that device-guided slow breathing has not been directly compared with other forms of regulated breathing such as pranayama. Hence, it remains unknown whether paced slow breathing can be taught and effectively used to lower BP over the long term without the use of a device.

According to trial evidence, 15-minute sessions of device-guided slow breathing need to be performed at least 3 to 4 times per week to reduce BP. It has been suggested that more frequent use may lead to greater BP lowering; however further evidence is required in this regard. There have been no trials longer than 8 to 9 weeks' duration; hence, the efficacy of long-term use is unclear. Longer and larger studies are also required to demonstrate the patient populations most likely to benefit from this technology.[88,89,110,111]

The writing group conferred to device-guided breathing a *Class IIA, Level of Evidence B* recommendation for BP-lowering efficacy. Device-guided breathing is reasonable to perform in clinical practice to reduce BP. Should additional studies in larger and broader populations corroborate its effectiveness thus far demonstrated, it is conceivable that this technique may merit even stronger recommendations in the future.

Exercise-Based Regimens

Numerous studies have evaluated the effects of various exercise modalities on BP. For the purposes of this review, exercise is characterized as predominantly dynamic aerobic, dynamic resistance, and isometric resistance. Dynamic (isotonic) refers to the regular, purposeful movement of joints and large muscle groups compared with isometric exercise, which involves static contraction of muscles without joint movement. Aerobic versus anaerobic describes the availability of oxygen for energy production during contraction and is typically a function of the relative intensity of exercise. Most activities involve a combination of many of these factors. Classification is typically done by the dominant characteristics of the exercise. Some trials have used single exercise types, and others have investigated the effects of combination regimens. Although the writing group acknowledges this complexity and the large variations among published studies, the BP-lowering actions of exercise are reviewed in the context of the dominant regimen type used in the studies.

It is important to emphasize that exercise regimens, in particular resistance training,[112] are contraindicated by existing guidelines in unstable cardiovascular conditions including the presence of uncontrolled severe hypertension (BP ≥180/110 mm Hg)[112,113] at least partially because of the transient incremental elevation in BP. Individuals with stage II hypertension (160–180/100–110 mm Hg) require assessment of their cardiovascular risk before beginning exercise training, as well as careful follow-up.[112–114] Additional recommended scenarios for performing stress testing before starting exercise programs have been outlined previously.[113]

Dynamic Aerobic (Endurance) Exercise

Aerobic training refers to exercise that is the dynamic regular and purposeful movement of large muscle groups in moderate and/or vigorous activity that places stress on the cardiovascular system. Usual examples of aerobic training exercises include speed walking, jogging, running, dancing, cycling, swimming, and using elliptical machines. The amount of aerobic exercise is measured as the intensity compared with rest, conveyed in metabolic equivalents (METs), equal to 3.5 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$ (eg, walking at 3 miles/h=3.5 METs, jogging at a 14-min/mile pace=6 METs, and jogging at a 10-min/mile pace=10 METs); duration (minutes per session); and frequency (number of sessions per week). The total amount of dynamic aerobic activity can be expressed as "exercise volume," which is the product of average METs multiplied by the number of minutes per week, with the goal of reaching 500 to 1000 MET·min/wk.

The general recommendations for exercise to improve health have been outlined in detail elsewhere.[115] They are not provided specifically for the treatment of hypertension but are suggestions on how to prescribe an exercise program according to an individual's habitual physical activity, physical function, and health status. An earlier position stand published in 2004 by the American College of Sports Medicine provided guidelines specifically on an exercise prescription plan for the treatment of hypertension.[114] The guidelines recommended ≥30 minutes of accumulated physical activity per day on most days per week. Moderate endurance physical activity at 40% to 60% maximum capacity was promoted with resistance exercise added as a supplement.

Meta-Analyses or Reviews

Physical fitness has been recommended for managing hypertension for >40 years.[116] Numerous individual studies have been performed, with the overall evidence supporting a clinically meaningful BP-lowering action of dynamic aerobic exercise. The most recent meta-analysis of endurance training (walking, jogging, running, cycling) published in 2007 involved 72 trials and 105 study groups with an average of 40 participants in the trials. The median age of participants was 47 years (57% male). On average, the participants were relatively fit, with a baseline peak energy expenditure of 9.6 METs, which increased by ≈1 MET after training. The median training consisted of 40-minute episodes performed 3 times per week over 16 weeks at an average intensity of 65% of heart rate reserve (maximal minus resting heart rate). After adjustment for the number of trained participants, exercise

induced significant net reductions in resting clinic (3.0/2.4 mm Hg; $P<0.001$) and daytime ambulatory (3.3/3.5 mm Hg; $P<0.01$) BPs.[117] The reduction in resting clinic BP was more pronounced among the 30 individuals with hypertension (−6.9/−4.9 mm Hg) compared with the individuals without hypertension (−1.9/−1.6 mm Hg; $P<0.001$). Overall, there was no observed effect of several exercise-related variables, including training frequency, intensity, and mode, as well as time per session, on the magnitude of BP response; however, the individual studies were not specifically designed in most instances to assess the effect of these factors.

A review published in 2010 evaluated the effects of regular aerobic exercise on BP levels assessed throughout the full 24-hour period measured by ABPM.[118] The overall findings were consistent with the previous meta-analyses of clinic-based BP measurements. Aerobic training was shown to reduce most ambulatory BP outcomes among individuals with hypertension in most studies. Nevertheless, it was noted that the responses were highly variable among individuals.

The effect of walking programs on BP was recently reviewed in 2010.[119] Nine of 27 trials (34% of the total participants) reported significant reductions in systolic or diastolic BP. It was noted by the authors that the trials that demonstrated a significant effect tended to be larger and used more intense and frequent (36.5-minute sessions performed 4.4 d/wk) exercise regimens for longer durations (19 weeks). Among the positive studies, the overall mean reduction in BP between the intervention and control groups from the baseline to the end of the follow-up ranged from 5.2 to 11.0 mm Hg and from 3.8 to 7.7 mm Hg for systolic and diastolic BPs, respectively. However, it was also noted that, as a result of heterogeneity and the limitations of the published studies, further high-quality trials are required to provide firm conclusions on the efficacy of walking programs.

Finally, in 2011, another systematic review evaluated the effectiveness of lifestyle interventions among women 18 to 44 years of age, with 5 studies examining the effects of exercise alone on BP.[120] The modes of exercise included aerobic interval training (AIT) and walking for 6 to 24 weeks' duration. Overall, there were nonsignificant changes in BP. As with so many exercise-based interventions, the sample sizes for these studies were relatively small (range, 21–53 women).

Recent Trials, Specific Patient Populations, and Different Exercise Programs

Many of the more recently published studies have investigated the effect of specific aspects of (eg, intensity) or variations in (eg, combined exercise approaches) the exercise regimen on the BP response after training. Additionally, the efficacy of aerobic exercise among several subgroups, including women, the elderly, and individuals with prehypertension, diabetes mellitus, metabolic syndrome, and kidney disease, has been reported.

The effect of exercise intensity on the resting and BP response to exercise after endurance training was recently reported among sedentary persons at least 55 years of age (22 individuals with normal blood pressure, 12 with prehypertension, and 5 with stage 1 hypertension). The study was a randomized crossover trial including lower-intensity (33% of heart rate reserve) and higher-intensity (66% of heart rate reserve) regimens, each performed for 10 weeks with an intermediary sedentary period. The exercise regimens consisted of 50-minute sessions performed 3 times per week. After training, systolic BP measured in the clinic decreased significantly and to a similar degree in both treatment arms: from 126.2±1.8 to 121.3±1.6 mm Hg after lower-intensity training ($P<0.05$) and from 125.4±1.8 to 119.7±1.5 mm Hg after higher-intensity training ($P<0.001$). Diastolic BP was reduced from 75.4±1.4 to 73.5±1.3 mm Hg and from 76.4±1.4 to 71.9±1.3 mm Hg after lower-intensity and higher-intensity training, respectively. The reduction in diastolic BP was significant only after higher-intensity training. BP decreased by 5.4/4.0 mm Hg in the 22 participants with normal BP at baseline and by 7.6/6.5 mm Hg in the 17 participants with high-normal BP or stage 1 hypertension ($P<0.01$). There was a similar reduction in systolic BP during submaximal exercise in both groups. However, mean day and nighttime ambulatory BP levels were not significantly altered after training, regardless of exercise intensity.[121] In contrast, in a study designed to assess the effect of exercise intensity in men with elevated ambulatory BP (mean, 145/85mm Hg), there was a graded additive BP-lowering effect on postexercise BP of more intense exercise. Over the course of the next 9 hours, compared with individuals in the control group, mean ambulatory systolic BP decreased 2.8±1.6 mm Hg after low-intensity (40% of peak $\dot{V}O_2$), 5.4±1.4 mm Hg after moderate-intensity (60% of peak $\dot{V}O_2$), and 11.7±1.5 mm Hg after vigorous (100% $\dot{V}O_2$ peak) exercise ($P<0.001$).[122]

Combining intermittent high-intensity (>80%–90% of maximal heart rate) with moderate-intensity (>60% maximal heart rate) aerobic training, known as AIT, has been shown to enhance fitness and weight loss and has been safely incorporated into cardiac rehabilitation in appropriate individuals. In 65 men and women with controlled hypertension, continuous and interval training performed in 40-minute sessions 2 times a week had a similar effect on ambulatory BP, but interval training decreased BP more than continuous training in those with 24-hour BP levels above the median at baseline (126/80 mm Hg). In addition, only higher-intensity interval training reduced arterial stiffness.[123] In a similar study, AIT was more effective than continuous training in stage 1 hypertension (mean ambulatory BP, 153/93mm Hg). After medication washout, 88 men and women were randomized to AIT or isocaloric continuous training for ≈40-minute sessions 3 times per week for 12 weeks. Ambulatory systolic BP was reduced by 12 mm Hg ($P<0.001$) by AIT and 4.5 mm Hg ($P=0.05$) by continuous training. Ambulatory diastolic BP was reduced by 8 mm Hg ($P<0.001$) by AIT and 3.5 mm Hg ($P=0.02$) by continuous training. Improved endothelial function as measured by flow-mediated dilation was observed only in the AIT group.[124]

Upper-limb aerobic exercise has also been shown to provide significant hemodynamic benefits among individuals with hypertension who are limited by orthopedic or vascular occlusive diseases. Twelve weeks of upper-limb cycling 3 times per week with progressive duration and intensity resulted in a significant decrease in systolic (134.0±20.0 to 127.0±

16.4 mm Hg; P=0.03) and diastolic (73.0±21.6 to 67.1±8.2 mm Hg; P=0.02) BPs, with no change among individuals in the control group. Arm exercise was associated with a significant improvement in small-artery compliance and endothelium-dependent vasodilation, each of which may help explain the decrease in BP.[125]

Aerobic exercise may also positively affect BP and left ventricular mass among individuals with borderline hypertension. In a recent controlled study of 52 middle-aged men with high-normal or mildly elevated BP, 16 weeks of stationary cycling 3 times per week for ≈45 minutes at 60% to 80% of maximum heart rate resulted in a highly significant reduction in resting BP (−12/−6.5 mm Hg) compared with individuals in the control group (−3/−1.1 mm Hg).[126] Most impressive was the marked reduction in postexercise BP among the exercise group after training (−29.2/−7.5 mm Hg) compared with the control group (−1/−1 mm Hg). Left ventricular mass also decreased significantly in the exercise group (−43.2±18.6 g), whereas there was no change among individuals in the control group (3.4±6.8 g; P<0.05).

The effect of brief bouts of exercise on ambulatory BP among individuals with prehypertension was evaluated in a randomized, crossover design in 21 men and women (mean age, 47.2±2.92 years).[127] There were 3 groups: accumulated physical activity of 10 min/h over a 4-hour period, 1 continuous 40-minute session (both at 50% of peak oxygen consumption), and a nonexercising control. Systolic and diastolic BPs were reduced for ≈10 hours after accumulated 40 minutes of exercise and for 7 hours after continuous exercise (P<0.05 for both). There were significant reductions in systolic (5.6±1.6 mm Hg; P=0.002) and diastolic (3.1±0.2 mm Hg; P=0.020) BPs in the group with accumulated physical activity, which was more effective in reducing systolic BP than a single continuous session (P=0.045).

There is some evidence that individuals with diabetes mellitus and/or chronic kidney disease can also achieve a reduction in BP from regular aerobic exercise. A randomized, controlled study involving participants with diabetes mellitus and chronic kidney disease compared aerobic exercise plus optimal medical management with medical management alone.[128] The exercise group underwent 6 weeks of supervised aerobic training 3 times weekly, followed by 18 weeks of unsupervised home-based exercise. After 24 weeks, exercise training resulted in increased exercise duration during treadmill testing and a decrease in resting systolic BP, although the decrease was not statistically significant, likely related to the small sample size (n=7). Another randomized, controlled study designed to assess the effect of exercise on a standard 6-minute walk test in end-stage renal disease compared the effects of 6 months of supervised intradialytic exercise training with home-based exercise training or usual care in individuals undergoing hemodialysis.[129] There were no statistically significant differences between intradialytic and home-based exercise or usual care for either the 6-mile walk or BP parameters. However, the sample size of the study was underpowered to attain statistical significance for the BP outcomes. Despite this limitation, the results supported a trend toward a reduction in BP by aerobic exercise among individuals undergoing dialysis.

In a recent study, 43 men and women (mean age, 50.2 years) with metabolic syndrome were randomized to 4 groups: AIT for 43 minutes 3 times per week with intervals of 70% to 95% at peak heart rate, multiple muscle group strength training for 40 to 50 minutes 3 times per week with resistance set at 60% of the participant's maximal weight for a given muscle group, a combination of AIT (twice per week) and strength training (once per week), or control (no change in dietary or physical activity patterns). A training effect on BP was noted in the AIT group (systolic and diastolic BPs reduced by 5.5 mm Hg [95% CI, −11.4 to 0.4] and 4.1 mm Hg [95% CI, −8.3 to 0.12], respectively, from baseline) but did not research significance in the 11 individuals.[130]

On the other hand, a modest increase in activity level may not be effective in lowering BP compared with dietary advice alone among individuals with diabetes mellitus. In the relatively large Early Activity in Type 2 Diabetes (ACTID) randomized trial of 593 newly diagnosed diabetics, individuals randomized to a pedometer-based program plus intense dietary counseling did not have significant reductions in systolic or diastolic BP after 6 to 12 months compared with those receiving standard or intense dietary advice alone.[131] The lack of BP lowering occurred despite increases in activity in the pedometer group (17% increase in mean steps taken daily). It was speculated that the exercise may have been of insufficient intensity or type (ie, did not also involve resistance training) to have improved BP.

In a randomized study, the effects of aerobic versus resistance exercise in men and postmenopausal women with prehypertension or stage 1 essential hypertension were evaluated.[132] Aerobic exercise was performed at 65% maximal oxygen consumption peak for 30 minutes 3 days per week, and resistance exercise comprised 3 sets of 10 repetitions at 65% of maximum 3 days per week. Among woman, there were greater BP reductions after resistance compared with aerobic exercise. Men, on the other hand, had comparable BP effects after either exercise mode. These data confirm the beneficial effects of both types of exercise for men and women and the potential need for tailoring nonpharmacological treatment plans for men and women with hypertension.[132]

In a large epidemiological study involving older male veterans (age, 65–92 years) with an 8-year median follow-up, an inverse and graded association between impaired exercise capacity (in METs) and all-cause mortality was noted.[133] Fitness categories were formed using the lowest 20th percentile of METs for this cohort (≤4 METs) followed by 1-MET increments for increases in exercise capacity (eg, 4.1–5, 5.1–6, and up to >9 METs). Mortality risk was 12% lower for every 1-MET increase in exercise capacity, regardless of age. Mortality risk was similar between least-fit individuals (≤4 METs) and those who achieved the next fitness category (4.1–5 METs), but thereafter, the risk declined significantly for the remaining fitness categories (P for trend <0.001). Importantly, systolic BP was significantly lower at higher fitness categories (P<0.001).

Further supporting the BP-lowering effects of aerobic exercise in older adults with hypertension is a trial conducted in 2010 involving men and women 76±8 years of age with stage

I isolated systolic hypertension.[134] Participants were randomized to 16 weeks of exercise consisting of aerobic training (progressive 40%–85% heart rate reserve) or strength training (resistance) 3 times per week or to passive control. Participants in the exercise groups had a significant decrease in diastolic (3 mm Hg; $P<0.05$) but not systolic BP.

Finally, a recent article published in 2012 has provided some of the first evidence that aerobic exercise training can effectively lower BP even among individuals with resistant hypertension, defined as a BP ≥140/90 mm Hg on 3 medications or a BP controlled by ≥4 medications.[135] Fifty individuals were randomized in a parallel-design study to participate (or not participate) in an 8- to 12-week treadmill exercise program 3 times per week. Aerobic activity was considered to be at a moderate level. Compared with individuals in the control group, 24-hour systolic (−5.4±12.2 versus 2.3±7.3 mm Hg; $P=0.03$) and diastolic (−2.8±5.9 versus 0.9±4.1 mm Hg; $P=0.01$) BP levels were significantly reduced by aerobic training.

Mechanisms of BP Lowering

Mechanistic studies provided evidence that the hypotensive effect of endurance aerobic training is probably mediated at least in part through a reduction in systemic vascular resistance via decreased activities of the sympathetic and the renin-angiotensin systems and improved insulin sensitivity. Many other factors, including improved endothelium-dependent vasodilatation, enhanced baroreceptor sensitivity, and arterial compliance, may also be involved.[117]

Summary and Clinical Recommendations

The majority of studies that have evaluated the effect of aerobic exercise training on BP have been limited by small sample sizes. There have been wide ranges of participant characteristics, basal fitness and BP levels, and exercise regimens investigated. Nonetheless, the overall available evidence and the results from the most recent meta-analyses support that moderate-intensity dynamic aerobic regimens are capable of significantly lowering BP among most individuals within a few months. The general health recommendation to perform moderate- or high-intensity exercise (>40%–60% maximum) for at least 30 minutes on most days per week to achieve a total of at least 150 minutes per week likely also applies to BP lowering.[115,117] Indeed, these guidelines agree with the American College of Sports Medicine position stand on exercise and hypertension.[114] In addition to the potential risks for musculoskeletal injuries, there is a small absolute short-term increase in cardiovascular risk induced by aerobic exercise, particularly after high-intensity episodes among unconditioned individuals and individuals with preexisting cardiovascular disease. The risk-to-benefit ratio and suggestions for performing exercise testing before endurance training is prescribed should be carefully considered as outlined in detail elsewhere.[113,114] Finally, further studies are required to elucidate the optimal mode, training frequency, intensity, and duration of exercise, as well as patient predictors of responses, that achieve maximal BP lowering. Therefore, we recommend following existing Joint National Committee guidelines to perform aerobic physical activity at least 30 minutes per day most days of the week.[4]

Because of the positive findings from the majority of trials and the meta-analyses, the writing group ascribed to dynamic aerobic exercise a *Class I, Level of Evidence A* recommendation for BP-lowering efficacy. Dynamic aerobic exercise should be performed by most individuals to reduce BP if clinically appropriate and not contraindicated.

Dynamic Resistance Exercise

Dynamic resistance exercises are forms of exercise in which effort is performed against an opposing force accompanied by purposeful movement of joints and large muscle groups. Dynamic resistance exercise involves concentric or eccentric contraction (shortening) of muscles. Common types include weight lifting and circuit training, often with the use of exercise equipment such as Nautilus-type exercise machines. These types of exercise are typically performed with a goal of progressively increasing muscle strength. However, such exercises might also have cardiometabolic benefits, including reduced BP.

Meta-Analyses or Reviews

The most recent meta-analysis of the effect of resistance training on BP was conducted in 2011.[136] The authors identified 25 trials (30 different interventions) that tested at least 1 dynamic resistance intervention. Of these 30 interventions, 12 were tested in individuals with optimal BP, 14 in those with prehypertension, and 4 in individuals with hypertension. The sample size of the trials ranged from 15 to 143 participants, with a total of 1043 adults across all studies. In general, trial reporting was of poor quality. For example, just 19 trials reported that outcome assessment was performed in a blinded fashion. Twenty-seven intervention arms used weight or training machines, 2 interventions used Dyna-Bands, and 1 trial did not report the type of exercise. The median duration of the interventions was 8 weeks (range, 6–52 weeks). The median frequency of exercise was 3 sessions per week (range, 2–3 sessions per week). In most trials, the exercise was performed in a supervised setting. Across all 30 groups, net mean changes in systolic and diastolic BPs were −2.7 mm Hg (95% CI, −4.6 to −0.78) and −2.9 mm Hg (95% CI, −4.1 to −1.7), respectively, with a random-effects model. There were no significant differences in the effects of the interventions stratified by baseline BP level. There were also no BP-lowering differences observed across various subgroups of individuals, nor was a relationship between training intensity and BP found. The authors recognized many limitations of their meta-analysis, including the overall paucity of trials and the poor quality of many of the individuals trials. Importantly, no detrimental effects on BP control or triggering of acute cardiovascular events was reported to be induced by resistance training.

It was later emphasized that BP was not the primary end point of interest in many of the studies included in the meta-analysis.[137] A separate meta-analysis of 9 studies with 11 treatment groups was presented. Resistance training yielded smaller BP-lowering effects (1.08/1.03 mm Hg) that were not statistically significant. In response, the authors supported their original findings, stating that there was

no evidence of publication bias or serious inconsistency across the studies.[136] They reanalyzed their data to include only studies reporting BP changes as the primary outcome. In 11 randomized trials (13 study groups), a smaller but still significant reduction was reported for systolic (−2.7 mm Hg; 95% CI, −4.8 to −0.54) and diastolic (−1.9 mm Hg; 95% CI, −3.3 to −0.54) BPs. There was no difference between studies measuring BP as a primary or secondary outcome.

Recent Trials

After publication of the meta-analysis, 2 relevant studies were published. One nonrandomized study assessed the effects of resistance exercise training on the occurrence of postexercise hypotension.[138] Findings from this study suggest that training might reduce the occurrence of such hypotensive episodes. Another study was a randomized trial that tested the effects of 2 doses of resistance training on BP and other outcomes in individuals in cardiac rehabilitation units who were concomitantly receiving aerobic training.[139] There were modest significant reductions in BP at the end of the intervention period; however, there was no control group. Hence, it is unclear if the interventions had any specific effect on BP.

Mechanisms of BP Lowering

The underlying pathway whereby resistance training reduces BP has received little attention. The few studies do not support consistent improvements in endothelial function,[140,141] arterial compliance,[140,142] sympathetic activity,[140,143] or changes in cardiac heart rate variability.[144] Some studies have even observed a worsening of arterial elasticity and aortic wave reflections.[145] Sex differences have been reported, with improved endothelial function without adverse changes in arterial stiffness after resistance exercise among women but not men.[132] Hence, the complex mechanisms linking dynamic resistance training to a small reduction in BP remain to be fully elucidated.

Summary and Clinical Recommendations

The overall evidence suggests that dynamic resistance exercise can lower arterial BP by a modest degree. The evidence base is notable for a lack of trials in individuals with hypertension. There are additional methodological limitations of the relatively few available studies. However, there is no evidence of harm, an acute triggering of cardiovascular events during exercise, or a chronic worsening of BP by dynamic resistance exercise from the available short-term studies. Hence, there is no rationale to contraindicate resistance training for most individuals with mild stage I hypertension.

As a result of the positive findings from the majority of trials and the meta-analyses, the writing group conferred to dynamic resistance exercises a *Class IIA, Level of Evidence B* recommendation for BP-lowering efficacy. Dynamic resistance exercise is reasonable to perform in clinical practice to reduce BP. Should additional studies in larger and broader populations corroborate its effectiveness thus far demonstrated, it is conceivable that resistance exercise may merit even stronger recommendations in the future.

Isometric (Resistance) Exercise

Isometric resistance exercise involves sustained contraction of muscles with no change in the length of the involved muscle groups. Most of the studies on isometric resistance were of short duration and enrolled relatively few participants. Nonetheless, a clear yet relatively small cardiovascular benefit of resistance training has emerged, including modest improvements in BP.[112]

Meta-Analyses or Reviews

There have been a few meta-analyses on the BP-lowering effects of isometric exercise. In 1 review published in 2010, the effect of isometric handgrip exercise training lasting at least 4 weeks was evaluated.[146] The main outcome showed an ≈10% decrease in both systolic and diastolic BPs (pooled from 3 studies including 42 and 39 individuals in the exercise and control arms, respectively). The exercise minus control group reductions in systolic and diastolic BP levels were −13.4 and −7.8 mm Hg, respectively. Although this change in BP was impressive, it is important to note that this analysis included only 3 studies and a small number of total participants. A more recent meta-analysis published in 2011 also evaluated the impact of several different resistance training modalities.[136] A subgroup analysis of isometric handgrip exercise alone showed larger decreases in systolic (−13.5 mm Hg; 95% CI, −16.5 to −10.5) and diastolic (−7.8 mm Hg; 95% CI, −16.4 to 0.62) BPs using random-effects analyses in the 3 included studies compared with dynamic resistance training (−2.7/−2.9 mm Hg). On the other hand, dynamic resistance exercise provided additional health benefits not observed in isometric exercise, including improved peak oxygen consumption, body fat, and blood triglycerides. However, this meta-analysis must be taken in the proper context given the heterogeneity of isometric training methods evaluated and the small number of individuals included in the studies. In this limited context, however, it provides support for the efficacy of isometric exercises, particularly handgrip, for lowering BP.

A few additional reviews of the BP-lowering efficacy of isometric handgrip exercises were published from 2008 to 2010.[147,148] Some studies not included in the previous meta-analyses for various trial quality reasons were also evaluated.[136,146] The overall conclusions of these reviews accorded with the findings of the meta-analyses. Many of the trials used a commercially available automated handheld dynamometer. However, a similar BP-lowering efficacy has been demonstrated by the use of an inexpensive spring-loaded handgrip device after 8 weeks of training in at least 1 randomized, controlled study of 49 individuals with normal blood pressure.[149] It was also noted that most of the protocols involving isometric handgrip necessitated less time commitment to produce effective reduction in BP (≈33 min/wk total) compared with other exercise modalities (eg, typically 150 min/wk with aerobic dynamic exercise).

Recent Trials

Several additional small studies have evaluated the BP-lowering efficacy of isometric exercise. In a study conducted in 2010, it was demonstrated that bilateral leg

Table 2. Class of Recommendation and Level of Evidence for Blood Pressure Lowering

Alternative Treatments	LOE	COR
Behavioral therapies		
Transcendental Meditation	B	IIB
Other meditation techniques	C	III (no benefit)
Biofeedback approaches	B	IIB
Yoga	C	III (no benefit)
Other relaxation techniques	B	III (no benefit)
Noninvasive procedures or devices		
Acupuncture	B	III (no benefit)
Device-guided breathing	B	IIA
Exercise-based regimens		
Dynamic aerobic exercise	A	I
Dynamic resistance exercise	B	IIA
Isometric handgrip exercise	C	IIB

COR indicates class of recommendation; and LOE, level of evidence.

isometric training can reduce resting BP.[150] In this study, 13 participants sat in a dynamometer that ensured a reproducible isometric exercise that allowed a 90° flexion of the hip while individuals sat in an upright position. Participants performed 4 bouts of 2-minute-long exercises separated by 3 minutes of rest, and great care was taken to have the participants exercise in a uniform fashion. Both systolic (−4.9±5.8 mm Hg) and diastolic (−2.8±3.2 mm Hg) BP levels were significantly reduced after 4 weeks of training.

In a similar study, individuals were randomized to a high- or low-intensity leg isometric regimen (≈10% and 20% maximum voluntary contraction, respectively) or to a control group.[151] This trial was carefully done but, again, included a relatively small cohort of only 33 healthy young male individuals. Exercise regimens consisted of 4 repeated 2-minute-long bouts performed 3 times weekly. Significant decreases in systolic, diastolic, and mean arterial BPs were seen at 8 weeks among both exercise groups. Although not statistically significant, the BP-lowering effects were slightly greater in the high- versus low-intensity exercise group (−5.2±4.0/−2.6±2.9 versus −3.7±3.7/−2.5±4.8 mm Hg, respectively). There were no significant changes in BP at the 4-week intermediate time point, which is different from the results in the previous study.[150] Although there was no effect of isometric exercise intensity on the degree of BP reduction, the difference in maximum voluntary contraction was small between groups.

Because of the paucity of clinical trials, numerous issues remain unresolved in terms of using isometric exercise training to maximize BP lowering, including the optimal intensities, muscle groups exercised, duration of therapy, number of static contraction bouts per session, and effect of training with bilateral versus unilateral muscle contractions. The effects across broader ranges of patient characteristics and initial BP values also require further investigation. Finally, the safety of using various isometric exercises and intensities among individuals with hypertension needs to be better evaluated. In particular, the cardiovascular health risks associated with the transient elevation in BP that occurs during muscle contractions need to be more clearly established. Few studies have investigated the magnitude of this BP surge among individuals with hypertension.[152] The available data suggest that the brief rise in BP can be quite pronounced, depending on the isometric exercise used (eg, percent maximal effort, size of muscle groups involved). On the other hand, the response is transient (ie, resolves within a few minutes), and there is no evidence from the few available published studies that it is associated with an increase in risk for acute cardiovascular events.[112,136,148] Nonetheless, isometric exercises have not been studied in very-high-risk or unstable cardiovascular patients or individuals with more severe levels of hypertension (eg, stage II). Careful and prudent restrictions on prescribing any type of exercise apply to individuals with uncontrolled BP. Current recommendations state that isometric exercise should be avoided among individuals with BP levels >180/110 mm Hg until their hypertension is better controlled.[112]

Mechanisms of BP Lowering

Isometric exercise causes an acute stimulation of the metaboreflex in a physiological attempt to restore muscle blood flow. This and other responses may produce reductions in tissue oxidative stress, improved vascular endothelial function, and favorable changes in baroreflex sensitivity, as well as autonomic balance over the long-term. The available studies provide mixed findings; thus, the responsible mechanistic pathways have not been fully clarified.[148]

Summary and Clinical Recommendations

The overall evidence suggests that isometric, particularly handgrip, exercises produce significant reductions in BP. However, caution is required at this point because only a few relatively small studies have been published. Results from larger-scale high-quality studies are necessary to draw firm conclusions. This would be of great benefit to the field because there may still be a concern among healthcare providers that isometric exercise is contraindicated because it acutely raises BP. The optimal methods of exercise also require further investigations. For the time being, following a program with published evidence that it can effectively lower BP is reasonable. In regard to isometric handgrip, this consists of several intermittent bouts of handgrip contractions at 30% maximal strength lasting 2 minutes each for a total of 12 to 15 minutes per session. This should be performed at least 3 times per week over 8 to 12 weeks.[147] Although no adverse events have thus far been reported (keeping in mind that most studies have used relatively low-intensity isometric exercises),[112,136,148] more data are needed to establish the safety of this modality.

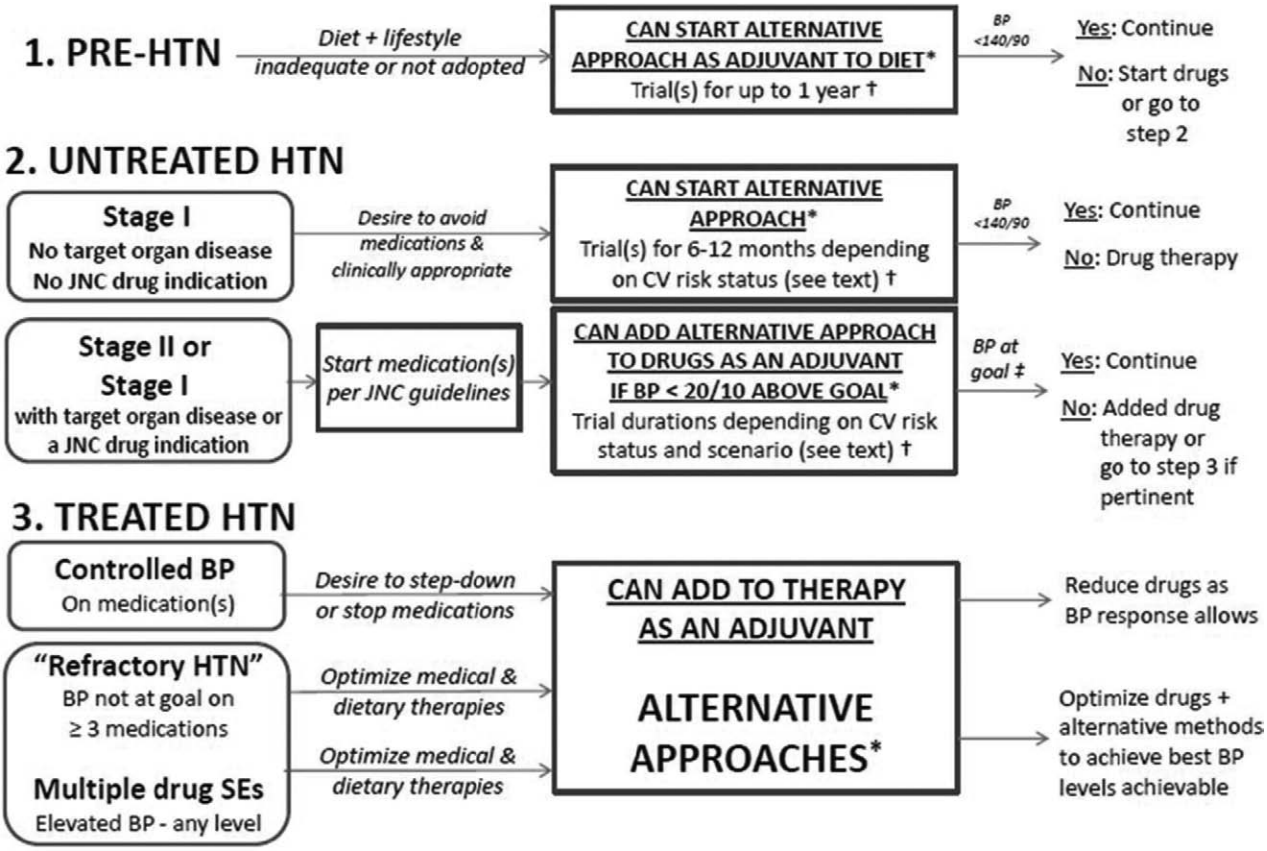

Figure. Algorithm for implementing alternative approaches in clinical practice. Target-organ disease is end-organ damage related to high BP (eg, left ventricular hypertrophy, chronic kidney disease, or albuminuria). See text for a detailed discussion of using this treatment algorithm in clinical practice. BP indicates blood pressure; CV, cardiovascular; HTN, hypertension; JNC, Joint National Committee VII on High Blood Pressure Management; and SE, side effect. *Start/assure compliance with dietary + lifestyle therapy. Individualize alternative approach with selection guided by Table 2. †Earlier medication therapy should be started (or added to existing therapy) if BP levels increase to >20/10 mm Hg above goals during this period. ‡Target BP depending on comorbidities per JNC guidelines.

On the basis of the review, the writing group ascribed to isometric handgrip exercises a *Class IIB, Level of Evidence C* recommendation for BP-lowering efficacy. Isometric handgrip exercise may be considered in practice to reduce BP. Should additional studies in larger and broader populations corroborate its effectiveness thus far demonstrated, it is conceivable that this technique may merit even stronger recommendations in the future.

Additional Alternative Approaches

During the past few decades, a wide variety of other nonpharmacological methods for lowering BP have been reported. Several promising approaches include endovascular radiofrequency renal nerve ablation,[153,154] baroreceptor activation therapy with carotid baroreceptor pacing,[155,156] and continuous positive airway pressure for individuals with sleep apnea.[157,158] Numerous additional approaches and complementary therapies have also been described.[16,159] These treatments are outlined in the **online-only Data Supplement—Methods and Results**. However, they were not systematically reviewed, and official CORs are not provided in this scientific statement because of the paucity of high-quality clinical trials, because of the investigational nature of the procedures, because they were considered a dietary approach (eg, nutraceuticals), or because the method pertains only to a selected set of individuals (eg, continuous positive airway pressure).

Clinical Practice Considerations

A summary of the ascribed LOE and COR values in relation to the BP-lowering efficacy of each modality is provided in Table 2. Dynamic aerobic exercise has a high LOE for BP lowering and the greatest potential for improving other cardiovascular health parameters (eg, lipids, glucose).[160] Numerous observational cohorts also suggest that it may reduce cardiovascular risk in a dose-dependent manner.[161,162] Therefore, aerobic exercise should be considered the primary alternative modality to help reduce BP. This recommendation accords with existing guidelines on using lifestyle modifications to treat prehypertension and stage I hypertension.[4] Resistance exercise also has a high LOE for BP lowering, has been associated with additional cardiovascular health benefits,[112] and is therefore also highly recommended by our review. The writing group endorses that most individuals should start with aerobic or resistance exercise (alone or together) as the first alternative approach unless contraindicated or they are unwilling or unable to exercise. This recommendation to incorporate resistance

exercise training for most individuals expands on existing BP guidelines that only explicitly promote aerobic activity.[4] However, the simple advice to individuals to adopt an exercise regimen is often met with modest and variable success.[18] A different or additional alternative modality may be used if BP proves unresponsive, if further treatment is needed to achieve goals, or if there is a lack of adherence to exercise. Among the approaches, it is the opinion of the writing group to next consider the use of device-guided breathing or isometric handgrip exercise. These modalities are recommended with a higher priority in the order of preference over the remaining options on the basis of the larger weight of evidence supporting their BP-lowering efficacy or their greater practicality to use in the real-world setting compared with the other techniques with a *Class IIB* recommendation (ie, TM and biofeedback).

General Role in BP Management

A large but variable body of evidence documents the ability of alternative therapies to lower BP, as reviewed in this scientific statement. We did not identify any consistently proven health risks posed by any of these treatments per se when used in a responsible manner and when BP levels are monitored appropriately. The exception to this rule is for clinicians to use caution when recommending exercise-based modalities for individuals with stage II hypertension and to proscribe them among individuals with severely elevated levels (>180/110 mm Hg) or unstable cardiovascular syndromes (eg, class III–IV angina) because of the associated transient increase in BP and cardiovascular risk, particularly during isometric and resistance exercises among unconditioned individuals.[18,112,113] It is also important to highlight that there is little to no evidence from randomized, controlled clinical trials that these therapies as a group can prevent hard cardiovascular events. Hence, the writing group believes that these alternative modalities should be considered adjunctive therapies to standard treatments (diet and medications) for high BP. Our recommended approach mirrors previous expert opinions for implementing dietary modifications among individuals with hypertension[10–12] and accords with the management principles for when and how to use nonpharmacological therapies in general as promulgated by nation-level guidelines.[4–6]

In summary, it is the consensus of the writing group that it is reasonable for all individuals with BP levels >120/80 mm Hg to consider a trial of alternative approaches as adjuvant methods to help lower BP. In light of the fact that there is little evidence that any alternative modality can reliably lower BP by ≥20/10 mm Hg, individuals requiring this magnitude of BP reduction (including untreated individuals with stage II hypertension) should use alternative approaches only after they are first treated with appropriate pharmacologic strategies. Individuals with an indicated medication per guidelines (eg, target-organ damage, underlying comorbidities) should also use these approaches only as supplements to the required drug therapy regardless of BP level.[4–6] It should also be emphasized that most alternative approaches reduce systolic BP by only 2 to 10 mm Hg. Hence, only a minority of individuals will be successful in reaching goals with these treatment modalities alone when BP is ≥10/5 mm Hg above target.

The choice of the specific alternative approach can be made on an individual-level basis. However, we recommend that this selection be guided by the evidence as outlined in Table 2. Moreover, it is critical that individuals are adequately educated by their healthcare provider on how to correctly adopt and implement their selected approach. For example, some modalities require practice and have been shown to be ineffective if not performed appropriately (eg, device-guided breathing).[92] In cases requiring special expertise (eg, exercise or meditation techniques, stress management) referrals should be made to providers with appropriate credentials or proficiency whenever possible. An overview of the recommended methods of how to use each alternative approach for BP lowering is addressed within each individual section (when available evidence exists). Individuals should also be clearly informed that unlike pharmacologically based treatments there is currently little to no evidence that these alternative approaches, besides exercise regimens, can prevent cardiovascular events to avoid engendering a false sense of security in this regard. Finally, there is no ostensible reason why >1 approach could not be carefully tried together; however, unlike the proven additive efficacy of lifestyle interventions (eg, Dietary Approaches to Lower Hypertension diet plus salt restriction or weight loss), whether combination alternative therapy yields incremental reductions in BP remains untested.[162]

BP Management Algorithm

A general approach for using alternative treatments is outlined in the Figure. In all circumstances, individuals should also be strongly encouraged at all visits to adhere to the dietary changes proven to lower BP.[10–12] There are several clinical scenarios likely well suited for using these alternative modalities. Individuals with prehypertension (ie, BP 120–139/80–89 mm Hg) are excellent candidates to help lower BP and possibly prevent the transition to overt hypertension.[19,20] Low-risk individuals with stage I hypertension (ie, BP 140–159/90–99 mm Hg with no target-organ disease [eg, proteinuria, left ventricular hypertrophy] or guideline indication for drug therapy for a specific comorbidity [eg, heart failure]) who wish to avoid medications are also reasonable candidates.[4–6] An alternative modality could be started in these groups after a trial of diet has proven inadequate, or they could be started concomitantly with dietary approaches initially. Among individuals already taking antihypertensive drugs, an adjuvant alternative treatment can be considered if clinically appropriate (eg, rapid BP reduction is not urgently required and if BP is <20/10 mm Hg above goal) to help avoid adding further medications. Other reasonable candidates include individuals who have controlled hypertension seeking to step-down or stop existing drug therapy,[163] individuals with persistent BP elevations despite maximal medical therapy (ie, refractory hypertension),[164] and those who have exhausted viable pharmacological options because of multiple drug intolerances.

The appropriate duration of treatment before assessing the final adequacy of BP response after initiating any alternative approach is not well established and depends on the individual situation. However, 3 months' duration is a reasonable time frame given that most of the approaches reduced BP among the studies within this period when shown to be effective. If the BP does not respond or reach target goals, a different alternative approach could thereafter be attempted if still appropriate for the clinical scenario. On the basis of guidelines, individuals with prehypertension can undertake nonpharmacological therapy (which should include these alternative modalities) indefinitely as long as their BP is followed up annually and does not progress to overt hypertension.[4–6] Individuals with stage I hypertension on initial assessment can consider trials for up to 6 months (individuals with other cardiovascular risk factors) or as long as 12 months (individuals without other cardiovascular risk factors).[4–6] If BP rises to levels consistently >20/10 mm Hg above goal during this treatment period or if individuals develop evidence of target-organ damage and/or an indication for a specific medication, appropriate pharmacological therapy should be started at that time. After the appropriate trial durations outlined above, if BP remains >140/90 mm Hg, most individuals should begin medication therapy. A final caveat to this algorithm is that most alternative treatments do not commonly reduce BP by >10/5 mm Hg. Close follow-up is warranted for individuals with BP levels this magnitude above target.

Research Recommendations

There are several shortcomings in our present knowledge of the merits of alternative BP-lowering modalities. These include a paucity of well-designed, high-quality cardiovascular outcome trials in appropriate populations with hypertension with adequate control intervention groups for a number of nonpharmacological interventions. The current scarcity of clinical trial evidence demonstrating that the typically modest reduction in BP associated with these approaches translates into a reduction in hard cardiovascular events is a major shortcoming. However, it must be acknowledged that event-based trials are unlikely to be conducted because of the prohibitive sample size required to demonstrate a benefit with small reductions in BP in relatively healthy individuals with mild hypertension. In the absence of such trials, one may have to rely on BP lowering per se as a widely accepted surrogate marker that reliably predicts the cardiovascular health benefits of a medical intervention.[1,25] Even small decreases in BP within a large population can translate into substantial public health benefits.[4–6] We therefore believe that the risk-to-benefit ratio favors reasonable recommendations for individuals to use these alternative approaches as long as they are used under appropriate circumstances and guidance by a healthcare provider. It is also important to re-emphasize that many of the reviewed alternative therapies (eg, resistance and aerobic exercise, yoga, meditation, acupuncture) may provide a range of health or psychological benefits beyond BP lowering or cardiovascular risk reduction.

The writing group has formulated additional specific recommendations for future studies to help better elucidate the potential clinical role of these methods. Given the enormous population of individuals with high BP levels above ideal who may be appropriate candidates for these treatments,[1,2] these issues warrant consideration. Future trials should assess BP changes by including home and/or ambulatory BP responses, which are known to be less variable, are associated with no (or a smaller) placebo effect, and are superior cardiovascular risk predictors than clinic readings alone. In addition, many of the modalities might appear spuriously effective when used briefly before measurement of BP in the clinic. On the other hand, modest reductions detected over a 24-hour period might be obfuscated by relying solely on clinic readings. The BP-lowering efficacy during long-term treatment (ie, ≥1 year) and the long-term compliance associated with these regimens remain largely unknown. Many nonpharmacological alternative regimens require significant motivation and perseverance for continued efficacy. The comparative BP-lowering efficacy across the various nonpharmacological regimens is another area that should be investigated, preferably within the same population to directly assess their relative effectiveness and tolerability. Whether certain characteristics (eg, demographics, biomarkers, or hemodynamic parameters) predict the degree of responses to the various treatments also remains unclear. The ability to optimally tailor specific modalities to match certain patient subtypes has not been explored. The effectiveness of combining alternative approaches together or with other dietary/lifestyle approaches is another important question yet to be adequately assessed. The capacity for these techniques to change the typically progressive course of BP elevations over time among individuals with mild stages or prehypertension has not been studied.[20] Special subgroups within the population, in particular the elderly, have generally been underrepresented in previous trials. Finally, the cost-effectiveness of using these modalities in clinical practice, particularly compared with dietary or medical approaches, in individuals with mild stages of hypertension or prehypertension remains to be determined.

Conclusions

Numerous alternative approaches for lowering BP have been evaluated during the past few decades. The strongest evidence supports the effectiveness of using aerobic and/or dynamic resistance exercise for the adjuvant treatment of high BP. Biofeedback techniques, isometric handgrip, and device-guided breathing methods are also likely effective treatments. There is insufficient or inconclusive evidence at the present time to recommend the use of the other techniques reviewed in this scientific statement for the purposes of treating overt hypertension or prehypertension.

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Lawrence J. Appel	Johns Hopkins Medical Institutions	None	None	None	None	None	None	None
John D. Bisognano	University of Rochester Medical Center	CVRx†	None	None	None	None	CVRx*	None
William J. Elliott	Pacific Northwest University of Health Sciences	None	None	None	None	None	None	None
Flavio D. Fuchs	Federal University of Rio Grande do Sul	None	None	None	None	None	None	None
Joel W. Hughes	Kent State University	NIH†	None	None	None	None	None	None
Daniel T. Lackland	Medical University of South Carolina	None	None	None	None	None	None	None
Gbenga Ogedegbe	New York University School of Medicine	None	None	None	None	None	None	None
Sanjay Rajagopalan	Ohio State University	None	None	None	None	None	None	None
Melvyn Rubenfire	University of Michigan	None	None	None	None	None	None	None
Beth A. Staffileno	Rush University Medical Center	None	None	None	None	None	None	None
Raymond R. Townsend	University of Pennsylvania	NIH/NIDDK†	None	None	None	None	Medtronic*; Novartis*; Pfizer*	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
George Bakris	University of Chicago	None	None	None	None	None	Abbott*; Takeda*; Johnson & Johnson*; Daiichi-Sankyo*; Relapsya*; Medtronic*	None
Brent M. Egan	Medical University of South Carolina	None	None	None	None	None	None	None
Clive Rosendorff	Mt. Sinai School of Medicine and the James J. Peters VA Medical Center	None	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

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AMERICAN HEART ASSOCIATION SCIENTIFIC STATEMENT:

Beyond Medications and Diet: Alternative Approaches to Lowering Blood Pressure

Online supplement: Methods and Results

ONLINE SUPPLEMENTAL METHODS

Systematic Review Search Strategies and Terms

Alternative BP-Lowering Approaches Sections of the document had search strategies using *PubMed* constructed for human and English language studies published between 1/1/2006 through 10/31/2011. The search strategy consisted of terms for a "HypertensionBase" (defined below) plus a "Clinical Studies (CS)/Systematic Reviews (SR) /Practice Guidelines (PG) base" (defined below). These 2 search bases were next combined with the corresponding search strategy for each treatment modality section (Sections A-C). Medical Subject Heading (MeSH) categories were used in the searches.

Hypertension Base

"Prehypertension"[Mesh] OR "Hypertension"[Mesh] OR "Blood pressure"[Mesh] OR hypertensi OR pre-hypertensi* OR prehypertensi* OR "Pre hypertensive" OR "pre hypertension" OR "high blood pressure" OR "elevated blood pressure"*

Clinical Queries Therapy/Broad OR Systematic Review

((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR random[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading]) OR* ***systematic [sb]****

Systematic Review search limit [sb]

(systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR (systematic review [tiab] AND review [pt]) OR consensus development conference [pt] OR practice guideline [pt] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice [ti] OR evidence synthesis [tiab])AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline [pt]))OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw]) OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [tiab] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw]))*
NOT (letter [pt] OR newspaper article [pt] OR comment [pt])

Section A

Main search method = HypertensionBase AND *Clinical Studies (CS)/Systematic Reviews (SR) /Practice Guidelines (PG) Base* AND BehaviorBase
Yielded = 124 English language human publications on 11/8/2011

Behavior Therapy Base (BehaviorBase)

"Relaxation Therapy"[Mesh] OR "Yoga"[Mesh] OR "Biofeedback, Psychology"[Mesh] OR "Tai Ji"[Mesh] OR "Stress, Psychological/prevention and control"[Mesh] OR "Stress, Psychological/rehabilitation"[Mesh] OR "Stress, Psychological/therapy"[Mesh] OR meditat OR "tai chi" OR "tai ji" OR "T'ai chi" OR yoga*

Section B
HypertensionBase AND CS/SR/PG base AND AcuBreathBase
Yielded = 105 English language human publications on 11/8/2011

Acupuncture Resperate/Breathing Base (AcuBreathBase)
"Breathing Exercises"[Mesh] OR "Acupuncture Therapy"[Mesh] OR "Acupuncture"[Mesh] OR "Massage"[Mesh] OR "Ultraviolet Rays"[Mesh] OR "Ultraviolet Therapy"[Mesh] OR "Steam Bath"[Mesh] OR acupuncture OR qigong OR "qi gong" OR "ch'i kung" OR "RESPeRATE" OR "device-guided breathing" OR ("device-guided" AND "breathing")

Section C
HypertensionBase AND CS/SR/PG base AND ExerciseBase
Yielded = 3090 (773 after review) English language human publications on 10/18/2011

Exercise Base
"Exercise"[Mesh] OR "Physical Exertion"[Mesh] OR "Physical Fitness"[Mesh] OR "Exercise Therapy"[Mesh] OR exercise OR ***(Exercise subtopics ORed together)***

ONLINE SUPPLEMENTAL RESULTS

BEHAVIORAL THERAPIES

Meditation Techniques

Contemplative meditation has most often been studied as Zen meditation or mindfulness meditation. Transcendental medication is based on meditative practices originating in Indian philosophic traditions and typically involves focused attention on a word, phrase, or concept to allow a state of awareness/consciousness.[1] Mindfulness meditation may be best described inculcating a non-judgmental awareness characterized by openness, acceptance, and reflection.[2] Meditation has been practiced for thousands of years and is associated with religious and cultural practices[3] such as Hinduism (as part of the Upanishads, part of Hindu scriptures and a treatise on the Vedas, Ashtanga Yoga and Hatha yoga) and Buddhism (i.e., mindfulness is the 7th step of the Noble Eightfold Path). Maharishi Mahesh Yogi popularized a version of meditation called Transcendental Meditation (TM) in the 1950's which is arguably the most studied meditative practice in regards to BP-lowering. Mindfulness meditation has also been incorporated into a group stress management intervention by Jon Kabat-Zinn, when he founded the Mindfulness-based Stress Reduction (MBSR) program at University of Massachusetts-Amherst to treat patients with chronic pain.[4]

Yoga

The term Yoga (Sanskrit meaning "union") originated in Hindu scriptures such as the Upanishads (ca.1500 BCE). In its truest sense, yoga incorporates physical, mental and spiritual elements with the goal of unifying these aspects. Patañjali (fl 150 BC), also the father of Ayurvedic medicine, wrote a treatise called the Yoga Sutras in which he formalized this discipline. Ashtanga yoga (Sanskrit, eight limbs) is the yoga of Patañjali and is composed of eight components: yama and niyama (moral and ethical restraints); asana (postures/positions); pranayama (breath control); pratyahara (internalization of the senses); dharana (concentration); dhyana (meditation); samadhi (mastery over the mind). The eight limbs can be viewed as eight levels of progress, each level providing benefits and laying the foundation for higher levels. Thus, the practice of yoga is intertwined with meditative and contemplative aspects that are inseparable. It is often emphasized that the physical yogic exercises are only a means to get the body ready for mental practices such as meditation. Hatha yoga is the other branch of yoga that in a sense focuses on the more physical aspects of the original eight limbs (asana, pranayama, pratyahara, dharana, dhyana and samādhi) again with ultimate goal of samadhi. Hatha Yoga differs

substantially from the Yoga of Patanjali in that it focuses on the purification of the physical body leading to the purification of the mind ("ha"), and "prana," or vital energy (tha). Compared to the seated asana, or sitting meditation posture of Patanjali's yoga, full body 'postures' are common in Hatha yoga. In the West, the term "yoga" is today typically associated with Hatha Yoga and its asanas (postures) as a form of exercise. In the 1960s, interest in Hindu spirituality grew throughout western nations, giving rise to a great number of schools. Among the teachers of Hatha yoga who were active in the west in this period were B.K.S. Iyengar (Iyengar yoga), K. Pattabhi Jois (Ashtanga- Vinyāsa) and Swami Satchidananda (Integral Yoga). A number of forms of yoga that primarily emphasize the callisthenic aspects of yoga have also gained traction in the west. These include “Power Yoga” which is a more vigorous asana practice and Bikram yoga which is primarily asanas practiced in hot temperature, which is not recommended for those with hypertension, especially individuals taking medications.

ADDITIONAL METHODS

Renal nerve ablation

The key role of the kidney and of the sympathetic system in the pathogenesis and maintenance of hypertension has long been recognized. Renal sympathetic efferent nerves influence the ability of the kidney to handle sodium-volume homeostasis and the afferent outflow promotes the sympathetic stimulation of other systems. Historically, radical sympathectomy was one of the only therapeutic methods for malignant hypertension, but this invasive surgery was fraught with serious adverse effects. More recently, the selective inhibition of the renal sympathetic nerve traffic by percutaneous catheter-based radiofrequency ablation has been explored. In a series of 50 patients with uncontrolled hypertension (systolic BP>160 mm Hg and taking at least 3 medications), BP was lowered by 27/17 mm Hg 12 months after sympathetic ablation.[5] In a follow-up study involving 153 patients with resistant hypertension the BP-lowering benefits were shown to be maintained over 2 years.[6] More robust evidence has recently been provided by a randomized controlled trial involving 106 patients with resistant hypertension.[7] The between-group difference of active treatment versus control in office BP at 6 months was 33/11 mm Hg ($P < 0.0001$). Thus far, few serious side effects and little evidence for long-term adverse consequences (e.g. renal artery stenosis) have been reported.

We were able to identify at least 15 registered in clinical trials aiming to test the efficacy of renal nerve ablation in hypertension and other disease states (e.g. heart failure).[8] Other benefits of the treatment reported thus far include improvements in OSA severity as well as insulin sensitivity.[9] These

findings have illustrated that renal sympathetic percutaneous ablation is a promising procedure to control systemic sympathetic efferent activity and as such may favorably affect other CV and metabolic diseases in addition to lowering BP. The results from ongoing larger clinical trials aiming to establish the efficacy and safety of this procedure over longer follow-up periods are awaited.

Carotid baroreceptor stimulation

Improvements in technology over the past decade have allowed for the programmable stimulation of carotid baroreceptors as a potential novel treatment option for resistant hypertension. The surgically implanted device consists of an internal programmable pulse generator, 2 electrode leads, and 2 field electrodes. The leads are positioned over the carotid sinuses bilaterally where electrical pulses are delivered (bilaterally or unilaterally as required) and intensified as needed to achieve the required BP-lowering. Initial studies showed promising results for this treatment modality termed baroreflex activation therapy (BAT).[10, 11]

Recently, the BP-lowering efficacy and safety of this device were investigated in a complex multi-center randomized clinical trial (phase III Rheos Pivotal Trial) among 265 patients with resistant hypertension.[12] After device implantation, one set of subjects started active BAT one month later while the second group was randomized to a delayed treatment limb with the device activated after six months. There were 2 BP-related co-primary endpoints. At the six month time point when the acute efficacy endpoint was evaluated, 54% of the participants of the initially-activated group and 46% of the non-active group reached the pre-specified endpoint of a drop of least a 10 mmHg in systolic blood pressure (P = 0.97). On the other hand, the sustained BP-lowering efficacy endpoint determined at month 12 did reach significance. The investigators cited several methodological limitations potentially explaining the negative results of the acute efficacy endpoint (e.g. unexpected reductions in BP after device implantation prior to randomization, larger than expected variability in BP changes and decreases in BP in the delayed BAT group during the first 6 months). Post hoc analyses evaluating the BP reductions in each limb compared to pre-implantation BP levels showed significant reductions in systolic BP at 6 months in the active versus delayed BAT (26 vs 17 mm Hg, p=0.03). However, there were also some concerning treatment-induced adverse events related to lead placement including transient (4.4%) or permanent nerve injury (4.8%), along with a 4.8% surgical complication rate. Overall, the results of this pivotal study were mixed. Future studies are planned that will employ improved technology (device miniaturization) along with a less invasive implantation procedures and

predominately unilateral carotid stimulation (which was shown to be successful for inducing BP-lowering among 75% of subjects in the pivot trial).

Continuous Positive Airway Pressure (CPAP)

Obstructive sleep apnea (OSA) has been identified as a risk factor for hypertension in many[13-15] but not all studies[16]. Excess adiposity is a strong risk factor for both hypertension and OSA and could serve as the underlying intermediate mechanism explaining the association between these comorbidities. On the other hand, OSA is a strong and independent risk factor for resistant hypertension[17, 18] and several animal and human studies have demonstrated a variety of direct mechanistic linkages between the pathophysiology of OSA and elevated BP.[19, 20]

The use of CPAP as a means to lower BP has been investigated by secondary analysis of various trials testing its efficacy in the treatment of OSA and in a few studies as the primary outcome. A meta-analysis of trials with office BP measurement identified a mean net decrease in systolic BP of 2.5 mm Hg (95% CI: 4.3 to 0.6) in patients treated with CPAP compared with control. The corresponding effect for diastolic BP was 1.8 mm Hg (95% CI: 3.1 to 0.6).[21] A meta-analysis of trials using ambulatory BP monitoring[22] demonstrated a discernable effect of CPAP as well (1.8 mmHg, 95% CI from 3.0 to 0.5 for 24-hour SBP and 1.8 (2.9 to 0.7) for 24-hour DBP).[22] A larger and more recent trial with ambulatory BP monitoring confirmed these results.[23] CPAP may also lower BP in patients with prehypertension and masked hypertension.[24] In a relatively small trial testing the efficacy of CPAP in patients with resistant hypertension,[25] 24 hour diastolic BP decreased significantly in patients treated with CPAP (4.9 ± 6.4 versus 0.1 ± 7.3mmHg in patients from the control group, P = 0.027).

The individual studies and meta-analyses show that though CPAP significantly lowers BP, on average the magnitude of reduction is clinically modest. However, it has been suggested that patients with higher levels of BP, those with refractory hypertension, and those with more severe OSA may derive more robust CPAP-related BP reductions.[19] Since the BP-lowering magnitude produced by CPAP is clearly less than that achieved with anti-hypertensive medications, as demonstrated in a recent randomized trial compared to valsartan therapy, the role of CPAP as a first line or primary method to treat OSA-related hypertension remains unjustified.[26] Nonetheless, CPAP is a viable additional modality to consider among patients with OSA and hypertension that may help lower BP modestly, ease hypertension control (particularly among those with resistant hypertension), and/or possibly reduce medication requirements.

Further Approaches

A limited number of studies have investigated the capacity of several additional treatments that could potentially lower BP. These include surgical decompression of the rostral ventral lateral medulla due to vascular contact or a mass lesion,[27] chiropractic manipulation of the first cervical vertebrae,[28] sauna and hot tub treatments,[29, 30] whole body ultraviolet light irradiation,[31] and enhanced external counter-pulsation therapy.[32] Each approach may hold some promise, at least among a sub-set of patients; however, practical limitations or a paucity of high quality trials remain limitations.

A wide variety of nutraceuticals, herbal remedies, and dietary vitamins or micronutrients have been touted to have a favorable effect upon BP.[33, 34] Some of the more widely studied or notable treatments include cocoa products,[35] garlic,[36] inorganic nitrates,[37, 38] and lactotripeptides.[39, 40] Additional agents with some and/or mixed evidence for BP-lowering effects include co-enzyme Q10, fish oil, L-arginine, tetrahydrobiopterin, alpha lipoic acid, glutamate, polyphenols, and Vitamin D supplementation.[33, 34] A complete review is beyond the scope of this scientific statement that focuses on approaches beyond "dietary" treatments. Futures larger or higher quality clinical trials are required to corroborate the clinical usefulness of each of these agents prior to them being recommended as viable approaches.

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