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Review article

Buddhist meditation for vascular function: a narrative review

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ABSTRACT

Background: High blood pressure represents an important risk factor for diseases related to cardiovascular system and is directly associated with high oxidative stress, inflammation and vascular endothelial dysfunction. Recently, there is promising data available to suggest that meditation-based low-cost and low-risk lifestyle modification strategies may provide beneficial effects on chronic inflammation, oxidative stress and maintenance of blood pressure, both in young and older adults. This review aims to summarize the evidence regarding the effectiveness of Buddhist meditation for vascular endothelial function and blood pressure.

Method: A search was conducted using Ovid MEDLINE, Scopus, CINAHL and PsycINFO for articles published from 1990 to 2018.

Results: Relevant articles (n = 407) were reviewed and 5 met selection criteria. Several lines of studies have provided compelling data showing that Buddhist meditation approach was effective in improving inflammation and vascular function (endothelial vasodilation and arterial stiffness) in both young and elderly cohorts. Particularly, Buddhist meditation approach has shown to be effective in reducing plasma inflammatory markers, increasing nitric oxide concentration and improving vascular endothelial function and glycemic control, which in turn can be favorable factors for demonstrated positive effects of Buddhist meditation on blood pressure and vascular function.

Conclusion: This paper presents brief overview of clinical outcomes of complementary therapeutic approach of Buddhist meditation in vascular function. In future, well-structured systematic reviews are essential to report specificity of Buddhist mindfulness-based approach on vascular function, blood pressure and other cardiovascular risk factors.

1. Introduction

Aging is associated with increased arterial stiffness, high blood pressure/hypertension and vascular dysfunction.[1,2] Many studies have provided evidence that both peripheral and central arteries are stiffer in subjects with mixed (systolic/diastolic) hypertension, compared with normotensive subjects.[3,4] Vascular dysfunction represents an important risk factor for cardiovascular diseases. Regulation of vascular function and high blood pressure status is mandatory to prevent future adverse events such as stroke, heart failure and myocardial infarction.[5] Similarly, aging is associated with high inflammatory status and oxidative stress. The advancing age-associated elevated inflammatory status has been reported to coexist in both sub-clinical and clinical status of cardiovascular disease including hypertension and vascular dysfunction.[6] Circulating inflammatory molecules are increased in hypertensive patients[7,8] and their levels even predict the onset of hypertension.[9,10] Epidemiological studies showed that the presence of chronic low-grade inflammation status can contribute to future development of hypertension.[11] Maintenance of vascular tone by endothelial function via nitric oxide (endogenous vasodilator) is one of the main factors in management of blood pressure and vascular function.[12] Decreased Nitric Oxide (NO) (endothelial-derived vasodilator) availability and increased inflammation and oxidative stress are reported as key elements in the impaired endothelial function, which is associated with advancing age.[13] Decreased NO levels can lead to changes in vascular tone by increasing arterial stiffness and blood pressure in older adults. High inflammatory

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status and oxidative stress associated with advancing age have been related to elevated levels of potent inhibitors of NO signaling pathway, such as Asymmetric Dimethylarginine (ADMA) and Thrombospondin-1 (TSP-1) via Endothelial Nitric Oxide Synthase (eNOS) (the enzyme critical for the generation and bioavailability of NO and endothelial function), causing malfunction in vascular endothelium (vascular endothelial dysfunction),[14–17] which could contribute to worsening of the related adverse cardiovascular conditions including high blood pressure. Moreover, presence of free oxygen radicals in the high oxidative stress can uncouple eNOS for further worsening of endothelial function.[18] Endothelial dysfunction has been associated with increased blood pressure in both animal and human studies.[19,20] Literature suggests that intima-media thickness (IMT; measure of arterial stiffness) is positively associated with ADMA levels,[21] which suggests the link between ADMA and increased blood pressure.

In recent years, complementary "mindfulness-based" meditation therapies and practices have become increasingly popular as strategies for a variety of cardiovascular risk factors. The term "mindfulness" refers to a conscious modality characterised by a state of mental presence and attention to the present moment.[22] Mindfulness-based techniques teach the capacity of discriminating thoughts, emotions and actions with positive effects from those with harmful effects. Growing body of evidence from mechanistic and clinical research studies have demonstrated favorable effects of the mindfulness-based meditation practices in decreasing cardiovascular risk factors such as hypertension,[23,24] lipid peroxidation and hyperlipidemia[25,26] and atherosclerosis.[27]

Mindfulness-based meditation is an old meditation practice rooted in Buddhism and it is widely practiced among Buddhist monks. Buddhist mindfulness strategies including Buddhist Vipassana and Anapanasati/breathing awareness meditation practices, has long been associated with spiritual development. The mindfulness-based stress reduction (MBSR) is a technique developed by J. Kabat-Zinn (in 1979) which is drawn on old Buddhist meditation practices, but adapts these practices in systematic way to suit Western cultures.[28,29] The Buddhist meditation approach is composed of the concentration on the breath (Anapanasati) or mindfulness of body, sensations, mind and mental phenomena (Satipatthana) or calm abiding (Samatha), which can lead to the subsequent relaxation.[30]

Breathing awareness meditation, which is comparable with Buddhist "Anapanasati" meditation technique (concentration on the breath), is widely used in practice as life-style modification approach for the management of hypertension and literature suggest positive effects of this approach in blood pressure management.[31,32] Recently, there is promising data available to suggest that Buddhist meditation-based interventions may provide beneficial effects on chronic inflammation, cardiovascular risk factors including vascular endothelial dysfunction and high blood pressure in both elderly and younger participants. Thus, the current narrative review presents overview of available clinical literature on effectiveness of Buddhist meditation on vascular endothelial function and blood pressure.

2. Method

Studies investigating effectiveness of Buddhist meditation approach for vascular endothelial function and blood pressure were identified by searching four online databases; Ovid MEDLINE, Scopus, CINAHL and PsycINFO for articles published from 1990 to 2018. Searches were conducted in February 2019 using combination of following search terms/phrases; "Buddhist meditation" OR "Buddhist mindfulness" AND "Vascular function" OR "Endothelial function" OR "Vascular endothelial function" OR "Endothelial dysfunction" OR "endothelium-dependent vasodilation" AND "Blood pressure" OR Hypertension OR "High blood pressure" OR "essential hypertension" OR "secondary hypertension" OR "elevated blood pressure" OR "Increased blood pressure" or "Primary hypertension". The review had two inclusion criteria. First, research study method should include core concepts of Buddhist meditation (Anapanasati or breathing meditation, Vipassana meditation, thoughtful walking meditation) and second, the primary outcome of the research must measure the changes of endothelial function or vascular function or blood pressure. Articles were published on Zen meditation technique and blood pressure or vascular function were excluded to keep consistency with the inclusion criteria. Literature reviews, conference abstracts and articles which were not published in English language were excluded.

3. Results

A total of 440 citations were identified by searching the electronic databases. Thirty three (33) duplicates were identified among the extracted total articles and excluded from the review. Four-hundred and seven (407) articles were selected for title and abstract screening and 401 articles were excluded as those articles were fallen into one of the following categories; non-relevant title or abstract, book chapters, review articles (narrative or systematic reviews or meta-analysis), conference proceedings or abstracts, protocol publications, editorials or commentaries. The remaining 6 articles were undergone full-text review. From these 6 articles, the article from Benson et al.,[33] was excluded as the article only summarises results from three case reports. Most studies had a quantitative randomized controlled study design (4/5),[34–37] one study is uncontrolled observational study (Saeloo et al. 2012).[38] All of the studies were conducted in Asia (Thailand (4/5)[35–38]; China (1/5)).[34] Out of five studies which were selected with randomised nature, the study by Sudsuang et al.,[37] is a quasi-experimental study, but the randomization procedure was not clearly described in the article.

The 5 selected studies comprised of both young and old adults (total 219) with hypertension (n = 9), type 2 diabetes (n = 23), depression (n = 45) and healthy young adults (n = 142). Age of the study samples range from 18 to 90 years.

Table 1 presents study characteristics and results of the 4 randomize controlled studies included in the review.

Buddhist meditation approach to high blood pressure (hypertension) and vascular function

Buddhist meditation technique has been shown to produce favourable effects on blood pressure. A pilot single-arm nurse-led study carried out in older patients (n = 12) who were medically diagnosed for primary hypertension demonstrated that self-healing Buddhist meditation was able to maintain blood pressures of these hypertensive participants below 140/90 mmHg and reduced stress levels.[38] However, the limitations of this study was that it did not include a control arm and that the sample size was small.

Few other randomized clinical trials which were conducted in old patients with cardiovascular risk factors demonstrated that Buddhist walking meditation and breathing meditation-"Anapanasati" were effective in reducing blood pressure and improving vascular function.[35,36]

A randomised intervention study conducted in older patients with mild-to-moderate depressive symptoms by Prakhinkit et al.[35] demonstrated significant reductions in blood pressure (systolic/diastolic) levels in response to 12-week Buddhist walking

Table 1
Summary of studies on Buddhist meditation for vascular function.

Author (year)[Ref] Design	Condition Age (years)	Intervention (regimen)	Outcomes and results	Conclusion
Chen (2013)[34]	60 first-year healthy nursing students;	(A) Buddhist meditation (mindfulness, 30 min daily for 7 days, n = 30));	1) SBP: ES = 0.08, p = 0.034; DBP: ES = 0.02, p NS	"Buddhism- based mindfulness meditation was beneficial for lowering SBP"
RCT	A: 19.4; B: 19.7	(B) Routine daily activities (no intervention, routine daily activities, n = 30)	2) HR: ES = 0.03, p NS	
Prakhinkit (2014)[35]	40 participants with mild-to-moderate depressive symptoms;	(A) Buddhist walking meditation (Weeks 1-6: Mild intensity exercises, 20 min, 3 times a week; Weeks 7–12: Moderate intensity, 30 min, 3 times a week; n = 14), plus aerobic walking exercise,	1) SBP: A vs. B (p not given)),A vs. C ($p < 0.05$); DBP: A vs. B (p not given), A vs. C ($p < 0.05$);	"Buddhist walking meditation was effective in . . .improving vascular reactivity . . ."
RCT	A: 74.0; B:74.8; C: 81.0	(B) Traditional walking (Aerobic walking exercise only, n = 13), (C) Sedentary control (Routine daily activities only, n = 13)	2) HR: A vs. B (not given), A vs. C (p NS); 3) Vascular activity and arterial stiffness: Resting brachial diameter: A vs. B ($p < 0.01$), A vs. C ($p < 0.01$); Peak brachial diameter: A vs. B ($p < 0.01$), A vs. C ($p < 0.01$); FMD: A vs. B (p NS), A vs. C ($p < 0.01$); Peak shear rate: A vs. B (p NS), A vs. C ($p < 0.01$); NO level: A vs. B (p NS), A vs. C ($p < 0.05$);	
Gainey (2016)[36]	23 patients with type 2 diabetes	(A) Buddhist meditation plus aerobic walking exercise (30 min daily, 3 times weekly for 12 weeks, n = 12)	1) SBP: A vs B ($p < 0.05$); DBP: A vs B ($p < 0.05$);	"Buddhist walking meditation produced favourable effects on blood pressure, arterial stiffness and blood cortisol level . . ."
RCT	A: 58; B: 63	(B) Aerobic walking exercise (30 min daily, 3 times weekly for 12 weeks, n = 11)	2) HR:A vs B (p NS) 3) Vascular activity and arterial stiffness: FMD: A vs B (p NS); baPWV: A vs B (p NS); ABI: A vs B (p NS); Basal brachial diameter: A vs B (p NS); Peak brachial diameter: A vs B (p NS);	
Sudsuang (1991)[37]	82 healthy male students	(A) Buddhist meditation (Dhammakaya, 4 hrs daily for first 3 weeks, 2 hrs daily for week 4 to 6, n = 52)	1) SBP: 3 week, A vs B ($p < 0.01$), 6 week, A vs B ($p < 0.01$); DBP: 3 week, A vs B ($p < 0.01$), 6 week, A vs B ($p < 0.01$);	". . .Buddhist meditation produces beneficial effects on blood pressure, autonomic nervous system function. . ."
Non-RCT	20-25 yrs	(B) Routine daily activities (not practiced meditation, n = 30)	2) PR: 3 week, A vs B ($p < 0.01$), 6 week, A vs B ($p < 0.05$);	

ABI, Ankle-brachial index; baPWV, Brachial-ankle pulse wave velocity; DBP, Diastolic Blood Pressure; ES, Effect size; FMD, Flow- mediated dilation; HBP, high blood pressure; HR, Heart Rate; hr, hours; NO, Nitric oxide; NS, Not significant; PR, pulse rate; PWV, Pulse wave velocity; RCT, Randomised controlled trial; SBP, Systolic Blood Pressure.

meditation and traditional walking intervention. Similarly, both groups demonstrated improvements in brachial artery structure and function. Flow-mediated dilatation (FMD), which is a marker of endothelial dependent vasodilatation, peak brachial diameter and peak shear rates were significantly improved in both intervention groups, however, resting brachial diameter only improved significantly in Buddhist meditation group. FMD was improved from $6.5 \pm 0.8\%$ to $12.2 \pm 1.3\%$ after 12 weeks of Buddhist meditation exercise whereas traditional walking exercise improved the FMD only from $5.3 \pm 1.2\%$ to $9.1 \pm 1.3\%$. The outcome of this study further demonstrated that improvements of resting brachial diameter and FMD in Buddhist meditation group were significant against the pre-intervention values and against the post values of sedentary control group,[35] which shows superior effects of Buddhist walking meditation on endothelial dependent vasodilatation than the traditional walking exercises.

Another randomized control study by Gainey et al.[36] showed that Buddhist walking meditation improves endothelium-dependent vasodilation in adult patients with type 2 diabetes. Significant reductions in both systolic and diastolic blood pressure levels were only observed in the Buddhist walking meditation group compared to the traditional walking exercise group. This could be further explained by significant improvements in arterial stiffness response to the Buddhist walking meditation. Brachial-ankle pulse wave velocity, which is a marker of brachial arterial stiffness, was also significantly reduced only in the Buddhist walking meditation group. Increased arterial stiffness is a main factor for age-related increases in blood pressure. Thus, this study demonstrated the positive effects of Buddhist walking meditation on arterial stiffness and blood pressure of these old patients with type 2 diabetic mellitus. Flow mediated dilatation (FMD) was significantly improved in both exercise groups. This could be explained by the fact that the walking exercise component of both interventions-induced increase in peak blood flow and shear stress, which increase the endothelial-dependent nitric oxide (NO) production leading to vasodilatation.

Interestingly, the positive effects of Buddhist meditation on vascular function were not only limited to older adults, studies with young adult cohorts showed the similar improvements in vascular function and blood pressure.

Sudsuang et al.[37] demonstrated significant reduction in mixed blood pressure (systolic/diastolic) levels after practicing Buddhist meditation technique when compared to aged-matched control group with routine daily activities in a study of young age

(20–25 years) male participants. Another randomised control trial which studied mindfulness practice approach incorporated with traditional Buddhist cultural concepts has reported a significant reduction of post-study systolic blood pressure level in the meditation group compared to the pre-meditation levels. However, no significant change in diastolic blood pressure was found in this study.[34]

4. Discussion

The available literature demonstrates that Buddhist meditation-based practice could potentially reduce the stress levels and increase mindfulness levels, reduce the blood pressure and improve vascular endothelial function. Interestingly, the literature demonstrates that Buddhist meditation-based interventions have beneficial effects on chronic inflammation and psychological distress, which are confounding factors for development of high blood pressure and cardiovascular diseases. The psychological stress is suggested as one of major factors for development and prognosis of cardiovascular diseases[39,40] and vascular/endothelial dysfunction.[41] Autonomic nervous system dysfunction, increased lipid peroxidation and oxidative stress, elevated expression of inflammatory markers and endothelial dysfunction in psychological dysregulation have been proposed as possible mechanisms for the association between cardiovascular diseases and psychological stress.[42,43] A growing body of evidence suggests a positive correlation between psychological stress and increased production of free radicals and oxidative stress.[44,45] Increased lipid peroxidation in psychological imbalance status could be partially responsible for the link between psychological distress and cardiovascular diseases through elevating oxidative stress levels, increasing lipid peroxidation and free radical generation and inducing inflammatory status. Buddhist meditation practice has shown to reduce depressive mood in both young adults[34] and old patients diagnosed with depressive symptoms,[35] together with improvements in cardiovascular risk factors such as lipid metabolism, inflammation, vascular endothelial dysfunction and blood pressure in these patients.

Nitric oxide (NO) signaling pathway is the main mechanism in the vascular system which is responsible for maintenance of vascular tone and vascular endothelial function.[46] The elevated levels of free radicals and oxidative stress could cause endothelial dysfunction and vasoconstriction by inactivating biologically active NO, increasing accumulation of inhibitors of NO generating enzyme, eNOS and increased production of inflammatory molecules. Buddhist meditation approach has been shown to reduce inflammatory marker levels and increase NO availability in recent studies.

An intervention study conducted in older patients with mild-to-moderate depressive symptoms by Prakhinkit et al.,[35] demonstrated significant reductions of cortisol and interleukin-6 (IL-6) concentrations in Buddhist walking meditation group when compared to traditional walking and sedentary control groups. The increased levels of pro-inflammatory IL-6 and cortisol levels reported in this depressive participant cohort could be a result of depression-mediated acute inflammatory response, therefore, the positive outcome of this research demonstrates Buddhist meditation practice may be beneficial in managing psychological distress-mediated inflammatory status. Similar observations were reported in type 2 diabetes adult patient cohort by Gainey et al.[36] and in young adult cohort by Sudsuang et al. in 1991.[37] Buddhist meditation practice has demonstrated significant reductions of cortisol levels in these studies. Cortisol is a major stress hormone responsible for producing inflammatory response. An increase secretion of cortisol produces an inflammatory response, and may contribute to incident hypertension.[47] Literature suggests that nitric oxide has a role in cortisol-induced hypertension in humans. Some pilot studies demonstrated that suppression of nitric oxide system can partially be responsible for cortisol-induced hypertension in humans.[48] Therefore, the positive effects of Buddhist meditation on inflammatory status could be partially responsible for the observed blood pressure modification effects of Buddhist meditation approaches.

In addition to these beneficial effects, Buddhist meditation technique has shown favorable effects on glycemic control. Uncontrolled glycemic condition could be another source for elevated oxidative stress and inflammatory status. Therefore, one possible mechanism for the reported positive outcomes could be through effects of the meditation technique on psychological distress-mediated oxidative stress and inflammation.

The duration and frequency of the meditation practice are important factors to maintain the beneficial effects of the meditation as demonstrated by Sudsuang et al.[37] In their randomized control study, both blood pressure and serum cortisol levels were higher at week 6 than the week 3 of the meditation practice in participants who were not able to achieve the consistency of their meditation practice. Literature demonstrated that acute effects of meditation practice could not positively affect nitric oxide production.[25] The authors explained the demonstrated outcome possibly due to long recovery time of plasma NO precursor, arginine at the end of stress period.[49] Therefore, consistent extended meditation practice is required to maintain optimal NO bioavailability and beneficial effects on the vascular function.

However, other possible mechanisms could not be ruled out. Modulation of the autonomic nervous system by Buddhist meditation-based stress reduction could be another possible mechanistic axis which needs further investigation by well-designed future research studies.

The strengths of the intervention studies which were captured in the current review were randomized study design and data analysis strategies which possibly exclude addition of random bias to the final outcomes. However, research in Buddhist meditation and cardiovascular diseases is still in its initial phase and the findings are still inconclusive. The main limitations of the available Buddhist meditation studies include small sample sizes, short duration of intervention and being limited to certain ethnic groups.

Therefore, in future, well-designed large scale randomised controlled interventional trials are required to further determine the therapeutic benefits of this low-cost, low-risk meditation technique on inflammatory axis and endothelial dysfunction for improving vascular function and managing high blood pressure and other cardiovascular risk factors. Furthermore, such studies should assess feasibility and acceptance of the Buddhist meditation practice in wide clinical and ethnic settings.

The present paper should be considered as a short review to current overview of available clinical literature. Thus, in future well-structured systematic reviews will further evaluate mechanistic link behind the Buddhist meditation approach and vascular function improvements.

Author contributions

AA and DC conceptualized the study and wrote the manuscript; AA searched the literature; AA and DC reviewed and approved the final manuscript for submission.

Conflict of interest

No conflict of interest to declare

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Ethical statements

No ethical approval was required for this manuscript as this study did not involve human subjects or laboratory animals.

Data availability

The data supporting the findings of this study are available within the article.

References

1. Lakatta EG, Levy D. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part I: Aging arteries: A "set up" for vascular disease. *Circulation* 2003;107(1):139–46.
2. Franklin SS, Gustin IV W, Wong ND, Larson MG, Weber MA, Kannel WB. Hemodynamic patterns of age-related changes in blood pressure: the Framingham Heart Study. *Circulation* 1997;96(1):308–15.
3. Liao D, Arnett DK, Tyroler HA, Riley WA, Chambless LE, Szklo M, et al. Arterial stiffness and the development of hypertension: the ARIC study. *Hypertension* 1999;34(2):201–6.
4. Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, et al. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension* 2001;37(5):1236–41.
5. Kannel WB. Blood pressure as a cardiovascular risk factor: prevention and treatment. *Jama* 1996;275(20):1571–6.
6. Dinh QN, Drummond GR, Sobey CG, Chrissobolis S. Roles of inflammation, oxidative stress, and vascular dysfunction in hypertension. *Biomed Res Int* 2014;2014.
7. Schillaci G, Pirro M, Gemelli F, Pasqualini L, Vaudo G, Marchesi S, et al. Increased C-reactive protein concentrations in never-treated hypertension: the role of systolic and pulse pressures. *J Hypertens* 2003;21(10):1841–6.
8. Stumpf C, John S, Jukic J, Yilmaz A, Raaz D, Schmieder RE, et al. Enhanced levels of platelet P-selectin and circulating cytokines in young patients with mild arterial hypertension. *J Hypertens* 2005;23(5):995–1000.
9. Sesso HD, Buring JE, Rifai N, Blake GJ, Gaziano JM, Ridker PM. C-reactive protein and the risk of developing hypertension. *Jama* 2003;290(22):2945–51.
10. Niskanen L, Laaksonen DE, Nyyssönen K, Punnonen K, Valkonen V-P, Fuentes R, et al. Inflammation, abdominal obesity, and smoking as predictors of hypertension. *Hypertension* 2004;44(6):859–65.
11. Engstrom G, Lind P, Hedblad B, Stavenow L, Janzon L, Lindgarde F. Long-term effects of inflammation-sensitive plasma proteins and systolic blood pressure on incidence of stroke. *Stroke* 2002;33(12):2744–9.
12. Li H, Witte K, August M, Brausch I, Gödtel-Armbrust U, Habermeier A, et al. Reversal of endothelial nitric oxide synthase uncoupling and up-regulation of endothelial nitric oxide synthase expression lowers blood pressure in hypertensive rats. *J Am Coll Cardiol* 2006;47(12):2536–44.
13. Brandes RP, Fleming I, Busse R. Endothelial aging. *Cardiovasc Res* 2005;66(2):286–94.
14. Cooke JP. Does ADMA cause endothelial dysfunction? *Arterioscler Thromb Vasc Biol* 2000;20(9):2032–7.
15. Isenberg JS, Ridnour LA, Perruccio EM, Espey MG, Wink DA, Roberts DD. Thrombospondin-1 inhibits endothelial cell responses to nitric oxide in a cGMP-dependent manner. *Proc Natl Acad Sci* 2005;102(37):13141–6.
16. Tripepi G, Raso FM, Sijbrands E, Seck MS, Maas R, Boger R, et al. Inflammation and asymmetric dimethylarginine for predicting death and cardiovascular events in ESRD patients. *Clin J Am Soc Nephrol* 2011;6(7):1714–21.
17. Lopez-Dee Z, Pidcock K, Gutierrez LS. Thrombospondin-1: multiple paths to inflammation. *Mediators Inflamm* 2011;2011.
18. Schulz E, Gori T, Münzel T. Oxidative stress and endothelial dysfunction in hypertension. *Hypertens Res* 2011;34(6):665.
19. Kielstein JT, Bode-Böger SM, Frölich JrC, Ritz E, Haller H, Fliser D. Asymmetric dimethylarginine, blood pressure, and renal perfusion in elderly subjects. *Circulation* 2003;107(14):1891–5.
20. Isenberg JS, Wink DA, Roberts DD. Thrombospondin-1 antagonizes nitric oxide-stimulated vascular smooth muscle cell responses. *Cardiovasc Res* 2006;71(4):785–93.
21. Nanayakkara PW, Teerlink T, Stehouwer CD, Allajar D, Spijkerman A, Schalkwijk C, et al. Plasma asymmetric dimethylarginine (ADMA) concentration is independently associated with carotid intima-media thickness and plasma soluble vascular cell adhesion molecule-1 (sVCAM-1) concentration in patients with mild-to-moderate renal failure. *Kidney Int* 2005;68(5):2230–6.
22. Bodhi B. What does mindfulness really mean? A canonical perspective. *Contemp Buddhism* 2011;12(01):19–39.
23. Ponte PM, Feliu-Soler A, Solé-Villa M, Matas-Pericas L, Filella-Agullo D, Ruiz-Herrerias M, et al. Benefits of mindfulness meditation in reducing blood pressure and stress in patients with arterial hypertension. *J Hum Hypertens* 2019;33(3):237–47.
24. Shi L, Zhang D, Wang L, Zhuang J, Cook R, Chen L. Meditation and blood pressure: a meta-analysis of randomized clinical trials. *J Hypertens* 2017;35(4):696–706.
25. Kim D-H, Moon Y-S, Kim H-S, Jung J-S, Park H-M, Suh H-W, et al. Effect of Zen meditation on serum nitric oxide activity and lipid peroxidation. *Prog Neuropsychopharmacol Biol Psychiatry* 2005;29(2):327–31.
26. Schneider RH, Nidich SI, Salerno JW, Sharma HM, Robinson CE, Nidich RJ, et al. Lower lipid peroxide levels in practitioners of the transcendental meditation [registered sign] program. *Psychosom Med* 1998;60(1):38–41.
27. Manchanda S, Mehrotra U, Makhija A, Mohanty A, Dhawan S, Sawhney J. Reversal of early atherosclerosis in metabolic syndrome by yoga-a randomized controlled trial. *J Yoga Phys Ther* 2013;3(1):1.
28. Kabat-Zinn J. Mindfulness-based stress reduction (MBSR). *Constructivism Hum Sci* 2003;8(2):73.
29. Kabat-Zinn J. *Full catastrophe living, revised edition: how to cope with stress, pain and illness using mindfulness meditation*. UK: Hachette; 2013.
30. Bonadonna R. Meditation's impact on chronic illness. *Holist Nurs Pract* 2003;17(6):309–19.
31. Barnes VA, Pendergrast RA, Harshfield GA, Treiber FA. Impact of breathing awareness meditation on ambulatory blood pressure and sodium handling in prehypertensive African American adolescents. *Ethn Dis* 2008;18(1):1–5.
32. Adams ZW, Sieverdes JC, Brunner-Jackson B, Mueller M, Chandler J, Diaz V, et al. Meditation smartphone application effects on prehypertensive adults' blood pressure: dose-response feasibility trial. *Health Psychol* 2018;37(9):850–60.
33. Benson H, Malhotra M, Goldman RF, Jacobs GD, Hopkins PJ. Three case reports of the metabolic and electroencephalographic changes during advanced Buddhist meditation techniques. *Behav Med* 1990;16(2):90–5.
34. Chen Y, Yang X, Wang L, Zhang X. A randomized controlled trial of the effects of brief mindfulness meditation on anxiety symptoms and systolic blood pressure in Chinese nursing students. *Nurse Educ Today* 2013;33(10):1166–72.
35. Prakhinkit S, Suppapitiporn S, Tanaka H, Suksom D. Effects of Buddhism walking meditation on depression, functional fitness, and endothelium-dependent vasodilation in depressed elderly. *J Altern Complement Med* 2014;20(5):411–6.
36. Gainey A, Himathongkam T, Tanaka H, Suksom D. Effects of Buddhist walking meditation on glycemic control and vascular function in patients with type 2 diabetes. *Complement Ther Med* 2016;26:92–7.
37. Sudsuang R, Chentanez V, Veluvan K. Effect of Buddhist meditation on serum cortisol and total protein levels, blood pressure, pulse rate, lung volume and reaction time. *Physiol Behav* 1991;50(3):543–8.
38. Saeloo J, Hatthakit U, Nilmanat K. Development and evaluation of a self-healing nursing model using buddhist meditation to treat hypertension. *Pacific Rim International Journal of Nursing Research* 2012;16(1):64–77.
39. Skala JA, Freedland KE, Carney RM. Coronary heart disease and depression: a review of recent mechanistic research. *Can J Psychiatry* 2006;51(12):738–45.
40. Khandaker GM, Zuber V, Rees JM, Carvalho L, Mason AM, Foley CN, et al. Shared mechanisms between coronary heart disease and depression: findings from a large UK general population-based cohort. *Mol Psychiatry* 2019:1.
41. Cooper DC, Tomfohr LM, Milic MS, Natarajan L, Bardwell WA, Ziegler MG, et al. Depressed mood and flow-mediated dilation: a systematic review and meta-analysis. *Psychosom Med* 2011;73(5):360.
42. Nemeroff CB, Goldschmidt-Clermont PJ. Heartache and heartbreak—The link between depression and cardiovascular disease. *Nat Rev Cardiol* 2012;9(9):526.
43. Cohen BE, Edmondson D, Kronish IM. State of the art review: Depression, stress, anxiety, and cardiovascular disease. *Am J Hypertens* 2015;28(11):1295–302.
44. Wang L, Muxin G, Nishida H, Shirakawa C, Sato S, Konishi T. Psychological stress-induced oxidative stress as a model of sub-healthy condition and the effect of TCM. *Evid Based Complement Altern Med* 2007;4(2):195–202.
45. Sivoňová M, Žitňanová I, Hlinčíková L, Škodáček I, Trebatická J, Ďuračková Z. Oxidative stress in university students during examinations. *Stress* 2004;7(3):183–8.
46. Cannon RO. Role of nitric oxide in cardiovascular disease: focus on the endothelium. *Clin Chem* 1998;44(8):1809–19.
47. Hamer M, Steptoe A. Cortisol responses to mental stress and incident hypertension in healthy men and women. *J Clin Endocrinol Metab* 2012;97(1):E29–34.
48. Kelly JJ, Tam SH, Williamson PM, Lawson J, Whitworth JA. The nitric oxide system and cortisol-induced hypertension in humans. *Clin Exp Pharmacol Physiol* 1998;25(11):945–6.
49. Milakofsky L, Harris N, Vogel WH. Effects of repeated stress on plasma arginine levels in young and old rats. *Physiol Behav* 1993;54(4):725–8.