Review Article

Yoga and Cardiovascular Diseases – A Mechanistic Review

Praveen Murugesan

Department of Cardiology, All India Institute of Medical Sciences, New Delhi, India

Abstract

Yoga is an ancient Indian practice that involves the mind and body. It is a combination of physical exercises and postures with a focus on deep breathing and meditation. Yoga thereby promotes a healthy lifestyle which is one of the key factors in the prevention of various cardiovascular diseases. The practice of yoga might hence be effective in preventing the onset of these diseases. Yoga exerts its beneficial effects by favorable modulation of the autonomic system, reduction in oxidative stress, decreased inflammatory stress, improved endothelial function, and epigenetic changes. These changes might contribute not only to the prevention of cardiovascular diseases but also to delaying and preventing the onset of various modifiable cardiovascular risk factors. This review aims to delineate the possible mechanisms of the effect of yoga on cardiovascular health and its potential beneficial effects.

Keywords: *Cardiovascular diseases, mechanism, prevention, yoga*

Introduction

Yoga is an ancient Indian relaxation technique that constitutes a combined practice of various structured physical exercises along with breathing techniques and meditation. The global burden of cardiovascular diseases is steadily increasing with around 523 million cases worldwide, and cardiovascular diseases remain the leading cause of disease burden.[1] Since the fundamental structure of yoga revolves around physical activity and meditation, they essentially form the basis of a healthy life recommended both for secondary and primary prevention of various cardiovascular diseases.

The daily demands of modern life are high and this elicits a chronic "flight or fright" response, leading to increased sympathetic tone.[2] This response, when persistent, can lead to chronic psychological stress, resulting in anxiety and depression.[3,4] Chronic stress is also a proven risk factor for cardiovascular disease[5] [Figure 1]. It is important to note that 20% of patients with coronary artery disease (CAD) or heart failure experience depression, which is three times greater than the prevalence in the general population.[6,7] This makes the practice of relaxation techniques all the more important. Yoga has been shown to reduce stress and stress-related disorders in various studies and meta-analyses. Yoga is thought to increase parasympathetic tone,[8] which neutralizes the increased sympathetic tone caused by the stress response.

One of the beneficial effects of globalization is that Yoga is widely gaining acceptance worldwide, especially the modern forms – Iyengar Yoga, Hatha Yoga, Ashtanga Yoga, and Hot Yoga. There has been an exponential increase in published literature on Yoga in the last two decades. This review aims to elucidate the important physiological mechanisms that could likely attribute to the beneficial effects of yoga in cardiovascular diseases [Table 1].

Methods

Yoga in cardiovascular diseases was the focus of this literature review, which aimed to synthesize and evaluate previous research on the subject. To gather up-to-date literature on this subject, electronic databases such as PubMed, ScienceDirect, and Web of Science were meticulously examined. Yoga, breathing techniques, and relaxation techniques were some of the MeSH keywords utilized. To expand the data set, the author also looked through the reference lists of selected papers. Because it did not include any direct human participants, this study did not

Address for correspondence:
Dr. Praveen Murugesan, All India Institute of Medical Sciences, Ansari Nagar, New Delhi - 110 029, India. E-mail: praveenmaiims@gmail.com

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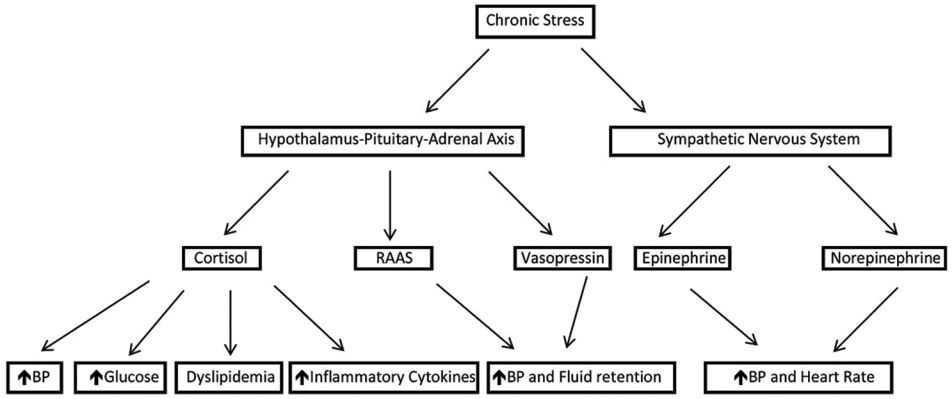

Figure 1: Deleterious effects of chronic stress

Table 1: Mechanism of the beneficial effects of yoga

Cardiovascular disease	Potential beneficial mechanism
Hypertension	Increased GABA production, decreased firing of the HPA axis, improved baroreceptor sensitivity, and decrease in oxidative stress
CAD and atherosclerosis	Reduced inflammation and oxidative stress
Arrhythmias	Increase in parasympathetic tone, reduction in ECM production, and atrial remodeling/ fibrosis. Improvement in QT dispersion
Heart failure	Decreased RAAS activation, reduced inflammatory and oxidative stress, and less symptoms due to improved lung function
Inflammation	Increase in parasympathetic tone and genetic and epigenetic modulations
Diabetes	Improved glucose utilization in skeletal muscles, increased beta-cell sensitivity, and increased beta-cell production

GABA: γ-aminobutyric acid, ECM: Extracellular matrix, HPA: Hypothalamus–pituitary–adrenal, RAAS: Renin–angiotensin–aldosterone system, CAD: Coronary artery disease

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Hypertension

Hypertension is one of the most important predictors of cardiovascular risk and is associated with significant mortality and morbidity.[9] The latest ACC/AHA guidelines recommend the promotion of optimal lifestyle habits in the general population to prevent the occurrence of hypertension.[10] For those who fit into the definition of elevated blood pressure (systolic blood pressure between 120 and 129 mmHg and with diastolic blood pressure <80 mmHg), nonpharmacological therapy is to be instituted for 3–6 months, before starting with pharmacotherapy. Nonpharmacological therapy includes a healthy diet, regular aerobic physical activity, smoking cessation, and weight loss.

Chronic stress is a significant risk factor for the development of hypertension in the long term.[11] The International Society of Hypertension recognizes this risk factor and recommends stress reduction by the incorporation of mindfulness and meditation in daily practice.[12]

Yoga has been shown to be beneficial in the reduction of blood pressure in various studies. One of the earlier studies conducted in the 1970s by Stone and DeLeo, Bleich, and Boro demonstrated the beneficial effects of relaxation techniques in lowering blood pressure.[13,14] Stone and DeLeo also demonstrated that in patients practicing relaxation techniques, the plasma levels of dopamine beta-hydroxylase levels were significantly lower, providing a mechanistic insight into reduced activation of the peripheral sympathetic system.[13] Hagins *et al*. showed that when all three elements (postures, meditation, and breathing) of yoga were practiced, it led to a reduction of SBP −8.17 mmHg and DBP −6.14 mmHg.[15] Overall, for every 10 mmHg lowering in systolic blood pressure, there is a 20% reduction in major cardiovascular events, 17% reduction in CAD, 27% reduction in stroke, 28% reduction in heart failure, and a 13% reduction in all-cause mortality.[16] Even short-term yoga practice has been shown to reduce blood pressure. In a randomized study by Murugesan *et al*., 3 months of regular yoga practice for 1 h a day was found to be as effective as drug therapy in lowering blood pressure.[17] Yoga can effectively act as a first line or add-on therapy in hypertension management. Furthermore, since there are no recommended therapies for the primary prevention of hypertension, incorporation of yoga into daily lifestyle could be a safe and simple measure to prevent the onset of hypertension.

Mechanism

The beneficial effect of Yoga in the reduction of blood pressure is attributed to its effect on the parasympathetic system in alleviating stress, a known causal factor for hypertension.[18] Acute stress causes activation of the hypothalamus–pituitary–adrenal (HPA) axis, which represents the first-line hormonal response toward the stressor challenge. However, chronic stress leads to

prolonged activation of the HPA axis which may lead to detrimental effects due to excessive sympathetic activity. The HPA axis activation has been shown to be a more prominent cause of hypertension.[19] Yoga practice increases the parasympathetic system and γ-aminobutyric acid system in the brain, decreasing the HPA axis.[20] In a novel randomized study by Kamei *et al*., the alpha wave activity of the brain was recorded, and blood cortisol levels were also measured simultaneously, and this was compared to the control group of nonpractitioners of yoga.[21] It was found that the two parameters were inversely correlated. In yoga practitioners, there was a significant increase in alpha wave activity and a decrease in serum cortisol levels. Yoga practice has been associated with an increase in cortical thickness and gray matter concentration. In a study by Afonso *et al*., there was increased cortical thickness in the left prefrontal areas in elderly long-term yoga practitioners.[22] The prefrontal area is responsible for planning complex cognitive behavior, personality expression, decision-making, and moderating social behavior. It is also thought that positive emotions are processed in the left prefrontal region. Another study showed that yoga practice resulted in an increase in the volume of the hippocampus, which plays an important role in memory.[23] These changes, overall, are attributed to the beneficial effects of yoga on the autonomic neurological function and an enhanced autonomic functioning may be attributed to the effect of reduction in blood pressure.

Another important mechanism of hypertension is an alteration in the baroreceptor sensitivity. In a study by Selvamurthy *et al*., yoga practice was shown to increase baroreceptor sensitivity and lower blood pressure.[24] A recent study by Christa *et al*. showed that yoga-based cardiac rehabilitation in postmyocardial infarction patients improved baroreceptor sensitivity and decreased blood pressure variability.[25] Yoga accompanied by a healthy food style has been shown to increase the urinary excretion of adrenaline, noradrenaline, dopamine, and aldosterone and increase the excretion of cortisol in a study by Schmidt *et al*.[26]

Oxidative stress is another risk factor that has been recognized for its casual role in hypertension.[27,28] In a study by Patil *et al*., yoga practice in hypertensive patients resulted in a significant reduction in serum malondialdehyde levels which is a marker of oxidative stress. Moreover, the levels of antioxidants like superoxide dismutase (SOD), glutathione, and Vitamin C were significantly elevated.[29] Overall, these positive effects of yoga help in the reduction of blood pressure.

Coronary Artery Disease and Atherosclerosis

CAD is one of the major cardiovascular diseases which leads to increased mortality and morbidity worldwide. Lifestyle measures must remain the foundation for the primary prevention of cardiovascular diseases. A healthy lifestyle has been shown to cause regression in coronary atherosclerosis. A landmark study by Ornish *et al*. showed that intensive lifestyle changes which included dietary measures, aerobic exercise, smoking cessation, and stress reduction in patients with established moderate-to-severe CAD, resulted in a significant reduction in atherosclerosis at the end of 5 years of study.[30] Yoga is shown to have mixed results in patients with CAD. In a randomized trial by Manchanda *et al*., yoga practice for 1 year in patients with angiographically proven CAD resulted in a significant reduction in plaque burden with regression of lesions.[31] There was also a significant reduction in the number of angina episodes, a reduction in body weight, and improved exercise capacity. In a similar study by Yogendra *et al*., yoga-based lifestyle modification resulted in regression of coronary lesions and improvement in myocardial perfusion index in patients with angiographically proven CAD.[32] Prabhakaran *et al*. showed that patients practicing yoga following acute myocardial infarction had improved self-rated health and returned to preinfarct activity after a short-term yoga therapy of 12 weeks.[33] However, this trial lacked statistical power to demonstrate differences in major adverse cardiovascular events. In another randomized trial that looked into the benefits of yoga as a part of cardiac rehabilitation in postacute coronary syndrome patients, the primary outcome of left ventricular diastolic function improvement by E/e', 6-min walk test, and blood pressure, heart rate, and estimated VO_2 max did not differ significantly in the yoga group versus the control group. However, this trial was limited by its small sample size of 80 participants with a short follow-up trial of 3 months.[34] Since acute coronary syndrome patients are at a higher risk with multiple comorbidities and risk factors, a longer period of yoga regimen may have been needed. In this trial, 78% of the patients were hypertensive, 38% were diabetics, and 19% were previously diagnosed with heart failure. These patients may have required a longer duration of yoga therapy. In conjuncture to this, a long-term study of postcoronary artery bypass patients, who underwent yoga therapy as a part of cardiac rehabilitation for 5 years, showed a significant improvement in quality of life and reduction in stress.[35] In a recent meta-analysis by Li *et al*., yoga was found to be associated with significantly improved quality of life as a secondary prevention strategy in CAD.[36]

Yoga also showed significant benefits in the reduction of carotid atherosclerosis. In a study by Fields *et al*., a multimodality natural medicine program, including yoga, showed a significant reduction in carotid atherosclerosis in older patients.[37] In a study that concentrated exclusively on yoga by Manchanda *et al*., yoga therapy for 1 year resulted in significant regression in carotid intimal thickness.[38]

Mechanism

The beneficial effects of yoga on atherosclerosis have not been clearly elucidated. Regression of atherosclerosis is thought to occur due to a reduction in psychosocial and oxidative stress

and inflammation. Relaxation techniques have also been shown to improve endothelial function in a few studies.[39] Yoga in postmyocardial infarction patients has also been shown to improve endothelial function by lowering endothelin-1, asymmetric dimethylarginine, vascular cell adhesion molecule vascular cell adhesion protein (VCAM), and intercellular adhesion molecule 1 (ICAM-1) levels.[40] Furthermore, other risk factors of atherosclerosis like hypertension and diabetes have been shown to have beneficial effects by yoga. This may lead to regression of atherosclerosis in the coronary arteries and other arteries.

Cardiac Arrhythmias

Arrhythmias are common in patients with heart diseases, with atrial fibrillation being the most common type.[41] Conversely, the presence of atrial fibrillation in patients with cardiac disease is associated with increased morbidity and mortality.[42] A new onset of atrial fibrillation is also associated with an increased risk of future coronary events.[43] Apart from these comorbidities, patients with atrial fibrillation also have significant impairment in quality of life.[44] Since the success rates of catheter ablation and anti-arrhythmic drugs are variable,[45] any alternate therapy that has a beneficial effect on atrial fibrillation will make a significant impact on the burden of atrial fibrillation.

Yoga has been shown to be beneficial in atrial fibrillation and attributed to stress reduction. One episode of anger or negative emotion is thought to increase the risk of atrial fibrillation by five-fold.[46,47] In a study by Lakkireddy *et al*., the practice of yoga for as many as 12 weeks has been shown to be associated with a significantly reduced number of episodes of atrial fibrillation in patients with paroxysmal atrial fibrillation.[48] Along with the reduction in atrial fibrillation episodes, yoga also significantly improves the quality of life and alleviates anxiety and depression in these patients. A review of yoga in patients with arrhythmias by Sharma *et al*. showed that yoga could be considered an adjunct therapy in reducing arrhythmias.[49]

Ventricular tachycardias are more prevalent in patients with CAD and those with heart failure.[50-52] Approximately half of the cardiovascular deaths occur suddenly,[53,54] with sustained ventricular arrhythmias being the most common cause.[55] QT dispersion is the marker of heterogenicity of ventricular repolarization which serves as a substrate for triggering malignant ventricular arrhythmias. Yoga has been found to be beneficial in improving QT dispersion. In a study by Dabhade *et al*., yoga was associated with significant improvement in QT dispersion when it was measured before and after the yoga session.[56] In a study by Prakash *et al*., deep breathing at 6 breaths per min resulted in a 50% reduction in VPC burden.[57] Long-term follow-up studies may provide more insights in this regard.

Heart rate variability is an important predictor of arrhythmic events. Reduced heart rate variability has been considered a single most important predictor of ventricular arrhythmias and sudden cardiac death.[58,59] Conversely, increased heart rate variability is associated with better cardiovascular outcomes. In a landmark study by Nolan *et al*., increased heart rate variability of SDNN >100 ms was associated with significantly reduced mortality in patients with heart failure.[60] Yoga has been shown to increase heart rate variability consistently across various studies.[58,61] Ghati *et al*. conducted the first randomized control trial which demonstrated the significant benefit of yoga in improving heart rate variability after a single session of yoga.[62]

Vasovagal syncope is common in the general population and is associated with significant deterioration in quality of life.[63,64] Management of vasovagal syncope has been challenging with the current drug therapy which includes beta blockers, mineralocorticoids, and alpha agonists showing mixed results. Physical counterpressure maneuvers have been beneficial as they increase the tone of the skeletal muscle thereby increasing venous return. Yoga, being a form of physical exercise, may be beneficial in patients with vasovagal syncope. In a study by Gunda *et al*., yoga therapy significantly reduced the number of syncope and presyncope episodes in patients with vasovagal syncope.[65] A recent randomized control study by Shenthar *et al*., in a similar population, also confirmed the benefits of yoga in vasovagal syncope with reduced burden and improved quality of life after 12 months of the study.[66]

Mechanism

Yogic breathing exercises cause the activation of stretch receptors in the respiratory system resulting in the activation of the vagal system.[67] It is also thought that stretch receptor activation above tidal volume results in sympathetic tone withdrawal in the peripheral blood vessels through the Hering–Breuer reflex.[68] The Om chant in yoga is also shown to be associated with increased vagal tone and limbic system activation.[69] These effects on the parasympathetic and sympathetic systems are thought to modulate the origin and occurrence of various arrhythmias. Activation of the sympathetic system can lead to overproduction of extracellular matrix production, upregulation of collagen production, increase in reactive oxygen species, transforming growth factor beta 1, and mononuclear infiltration which increases negative remodeling and atrial fibrosis.[70,71] Anxiety is also thought to increase the production of angiotensin II which can lead to increased left ventricular hypertrophy and atrial fibrosis.[72] Furthermore, emotional disorders are thought to activate ectopic rhythm from myocardial cells in the pulmonary veins near its opening into the atrium, which may predispose to atrial fibrillation.[73] Hence, the increased parasympathetic tone by yoga is thought to be the mechanism by which it reduces arrhythmias.

Myocardial infarction results in an area of muscle necrosis which is an area of relative absence of sympathetic

regulation. This is a functionally de-innervated area that has reduced vagal tone. This leads to nonuniformity in the refractory period of the myocardial which predisposes for ventricular ectopy. After myocardial infarction, nerve sprouting occurs in the affected areas mediated by neural growth factor. This sprouting of nerves results in sympathetic hyperactivity. This increase in sympathetic activity combined with the in-homogeneous tissue refractory period forms a substrate for ventricular arrhythmias and sudden cardiac death.[74,75] Yoga could be beneficial in the reduction and prevention of cardiac arrhythmias through its action parasympathetic system, endothelial function, and reduction in oxidative stress.

The beneficial effect of yoga in vasovagal syncope is thought to be its effects on the autonomic nervous system and venous tone. A sustained increase in venous tone is thought to occur with yogic posturing exercises.[66] Furthermore, an increase in parasympathetic tone is thought to counteract the exaggerated sympathetic activation of the C-mechanoreceptors.

Heart Failure

Heart failure is a rapidly growing disease with increasing prevalence worldwide.[76] Progression of heart failure is mediated by activation of the renin–angiotensin–aldosterone system (RAAS).[77] Exercise training programs are recommended along with medical therapy, as a part of the cardiac rehabilitation program to prevent the progression of heart failure.[78,79] Yoga may be beneficial in heart failure as it has been shown to decrease activation of RAAS and is also a form of physical therapy with varying metabolic requirements.

In a study on heart failure patients randomized to yoga versus standard therapy, yoga therapy resulted in a significant reduction in the inflammatory markers interleukins, C-reactive protein, and extracellular SOD. There was also a significant improvement in functional capacity and quality of life.[80] In a study by Kubo *et al*., yoga therapy resulted in a significant reduction in body weight and depression in a multiethnic population.[81] Krishna *et al*. showed that a 12-week yoga therapy in heart failure patients led to a significant reduction in heart rate and blood pressure.[82] Since hypertension is one of the major risk factors of heart failure worsening and hospitalization, a reduction in blood pressure may favorably alter the course of the disease. In another study by the same group, the effect of yoga on N-terminal pro B-type natriuretic peptide (NT-proBNP) in heart failure patients was observed.[83] There was a significant decrease in NT-proBNP levels after 12 weeks of yoga. Moreover, there was also a significant improvement in left ventricular ejection fraction. Chronic heart failure results in increased capillary pressure, which when persistently elevated can result in impaired diffusion capacity and alveolar conductance in the lungs.[84] Yadav *et al*. showed that the yogic breathing exercises in CAD patients led to significant improvement in vital capacity, peak expiratory flow rate, maximum voluntary expiration, and diffusion factor.[85]

Mechanism

The beneficial effect of yoga on heart failure is thought to be due to its effects on the RAAS system. Activation of the sympathetic nervous system and RAAS system is implicated in the progression of heart failure.[86] In this context, beta-blockers and angiotensin-converting enzyme inhibitors have shown mortality benefits in patients with heart failure, due to a reduction in the activation of these systems.[87,88] Yoga therapy could also lead to a reduction in left ventricular filling pressure due to a decrease in sympathetic activation.[89] Furthermore, the beneficial effects on blood pressure reduction could result in favorable outcomes in patients with heart failure. There is increased O_2 utilization due to muscle stretch caused by the posturing in yoga.[90] This may lead to an increase in VO_2 consumption, alleviate muscle fatigue, and improve functioning. Finally, improvement in baroreceptor sensitivity and parasympathetic tone may decrease the incidence of arrhythmias in patients with heart failure, which may contribute to beneficial outcomes.

Inflammation, Lipids, and Oxidative Stress

Inflammation acts as both a causal agent and a marker of atherosclerosis.[91] In the ATTICA study by Pitsavos *et al*., the presence of anxiety and stress was associated with significantly higher levels of inflammatory and coagulation markers, which included tumor necrosis factor-α, Interleukin-6, homocysteine, and fibrinogen levels.[92] Since yoga is a stress-reduction therapy, it may be beneficial in reducing inflammation, thereby preventing and halting the development of atherosclerosis. In a study by Chohan *et al*., the practice of yoga was significantly associated with a reduction in fibrinogen levels.[93] In a study by Pullen *et al*., an 8-week regimen of yoga in heart failure patients resulted in a significant reduction in inflammatory markers.[80]

Yoga has also been shown to have benefits on oxidative stress and lipid profile. In a study by Gordon *et al*., yoga therapy in patients with type 2 diabetes mellitus (T2DM) showed a significant reduction in oxidative stress as measured by lipid peroxidase and a reduction in total cholesterol and very low-density lipoprotein lesions.[94] A similar benefit in oxidative stress reduction was seen in a study by Damodaran *et al*. in patients with hypertension.[95] In a study by Mahajan *et al*., yoga intervention resulted in an improvement in lipid profile in individuals with dyslipidemia and other risk factors of CAD.[96] Yoga showed a significant decrease in all lipid parameters except high-density lipoprotein.

Mechanism

An increase in mindfulness and the feeling of well-being is thought to occur with regular yoga practice. This may

lead to a reduction in inflammatory markers and oxidative stress.[97,98] Yoga and relaxation techniques have been shown to reduce the expression of inflammatory genes by directly inhibiting them. In a study by Buric *et al*., the practice of relaxation techniques leads to reduced expression of the NF-κB gene.[99] Conserved transcriptional response to adversity (CTRA) is an immunological response to chronic stress which is characterized by the upregulation of inflammatory cells and downregulation of genes involved in Type 1 interferon response.[100] Furthermore, activation of this CTRA is thought to be associated with poor outcomes of chronic illnesses, including cardiovascular diseases.[101] Yoga and relaxation techniques have been shown to reduce the expression of this response.[99] Yoga has effects on posttranscriptional modification and epigenetics. Harkess *et al*. showed that yoga was associated with hypomethylation of the TNF gene, which is an important regulator of proinflammatory response.[102]

Diabetes and Metabolic Syndrome

Diabetes is one of the important risk factors for the development of cardiovascular disease. In the HA1C study by Bock *et al*., yoga was found superior to standard exercise therapy in patients with T2DM in reducing glycated hemoglobin (HbA1c) levels and quality of life at 6 months.[103] In a meta-analysis of 23 studies of diabetes and yoga intervention, yoga was found to have a significant effect in lowering HbA1c and postprandial blood glucose levels.[104] Yoga has also been associated with significant improvements in lipid profile, body mass index, and waist-to-hip ratio.

Metabolic syndrome comprises impaired glucose tolerance, hypertriglyceridemia, obesity, and hypertension. Weight reduction is known to occur in practitioners of yoga owing to posturing and metabolic activity. Studies have demonstrated a significant reduction in body weight, both in healthy individuals and in patients with established cardiovascular disease.[30,92] Since yoga has shown beneficial effects on all the individual parameters of metabolic syndrome, its effect on patients with metabolic syndrome is expected to be beneficial. This was seen in a randomized trial by Khatri *et al*., in which patients with metabolic syndrome were randomized to yoga versus usual care. There was a significant improvement in all parameters of metabolic syndrome after 3 months of the study.[105] A meta-analysis by Chu *et al*. showed that there was a significant positive effect of yoga on metabolic syndrome.[106]

Mechanism

Yogic asanas are thought to have a positive effect on glucose utilization and fat redistribution.[107] Improved blood supply to muscles may enhance insulin receptor expression in muscles and lead to increased glucose uptake.[108] Manjunatha *et al*. observed increased sensitivity of β-cells of the pancreas to glucose load, which has been sustained over a long term in those with regular practice of yoga.[109] Breathing exercises are also thought to regulate the pineal, pituitary, and adrenal glands which play an important role in the regulation of metabolism.[110] Chronic stress is a risk factor for insulin resistance and diabetes.[111] Stress reduction by yoga is thought to decrease the risk of diabetes occurrence. Furthermore, abdominal stretching during yoga exercises is believed to result in the regeneration of pancreatic cells.[112] The beneficial effects of yoga on metabolic syndrome are thought to occur due to its pleiotropic effects on individual parameters.

Device-based Therapy

Since the beneficial effects of yoga on the cardiovascular system are predominantly thought to occur through mediation of the parasympathetic nervous system, other measures to stimulate the parasympathetic nervous system could also replicate these beneficial effects. Implantable devices have been in development for many years. One of the earlier studies by Braunwald *et al*. showed that carotid nerve stimulation lead to a decrease in angina episodes in patients with CAD.[113] Baroreceptor in carotid sinus stimulation has led to a decrease in blood pressure and are useful in the management of hypertension.[114] Vagus nerve stimulation has been shown to improve left ventricular function in patients with heart failure.[115,116] Recently, a noninvasive method of vagus nerve stimulation transcutaneously over the tragus, to stimulate the auricular branch of the vagus nerve, has been developed. This has been shown to decrease sympathetic tone, increase heart rate variability, and prevent atrial remodeling.[117,118] These devices could have potential benefits in the future with the upcoming newer large-scale trials. Furthermore, randomized control trials on yoga therapy need to be pursued to provide more insights into the mechanisms and benefits of yoga in cardiovascular diseases.

Limitations and Future Perspectives

The major concerns in the available literature on yoga and cardiovascular diseases are the small sample size, heterogenicity in the technique practiced, lack of multicenter studies, the inclusion of surrogate endpoints, and a short follow-up period. Although mechanistic studies focused on the effect of yoga on cardiovascular diseases are available, the beneficial effects are often not reproduced by similar studies. Dedicated large randomized trials with pragmatic trial designs incorporating preventive cardiologists and yoga physicians would help uncover the true potential of yoga and other relaxation techniques. This would, in turn, lead to guideline recommendations on a patient-centered approach on the practice of yoga, pertaining to the specific yogic techniques, frequency, and duration.

Conclusion

Yoga, an ancient Indian form of meditation, which combines both mental and physical disciplines, has

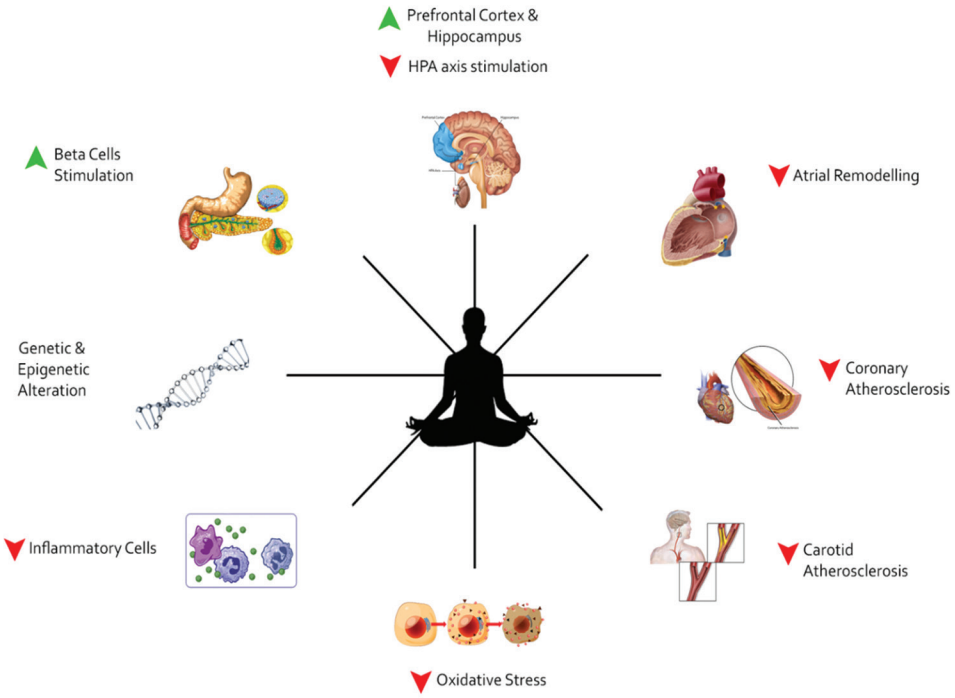

Figure 2: Pleotropic effects of yoga on various organ systems

demonstrated beneficial pleotropic effects [Figure 2]. It has been shown to demonstrate various favorable hemodynamic, anti-inflammatory, and autonomic changes. These changes are likely to be beneficial in the prevention and control of cardiovascular diseases and modifiable risk factors. However, the evidence base on yoga is still in its incipient stage. Large-scale studies are necessary to demonstrate the beneficial effects of yoga on more diverse and larger populations, particularly pertaining to cardiovascular diseases. Unlike other alternative medical therapies, yoga can be practiced in conjuncture with existing contemporary evidence-based medicine. Since yoga practice has not been associated with any major side effects, it is prudent to consider yoga as both a preventive and therapeutic measure in various cardiovascular diseases.

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Conflicts of interest

There are no conflicts of interest.

References

1. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, *et al.* Global burden of cardiovascular diseases and risk factors, 1990-2019: Update from the GBD 2019 study. J Am Coll Cardiol 2020;76:2982-3021.
2. Nesse RM, Bhatnagar S, Ellis B. Evolutionary origins and functions of the stress response system, stress. George Fink, editor. In: Concepts, Cognition, Emotion, and Behavior Handbook of Stress Series. Academic Press; 2016. p. 95-101. [doi: 10.1016/B978-0-12-800951-2.00011-X].
3. Iwata M, Ota KT, Duman RS. The inflammasome: Pathways linking psychological stress, depression, and systemic illnesses. Brain Behav Immun 2013;31:105-14.
4. Ventriglio A, Gentile A, Baldessarini RJ, Bellomo A. Early-life stress and psychiatric disorders: Epidemiology, neurobiology and innovative pharmacological targets. Curr Pharm Des 2015;21:1379-87.
5. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, *et al.* Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. Lancet 2004;364:937-52.
6. Ruo B, Rumsfeld JS, Hlatky MA, Liu H, Browner WS, Whooley MA. Depressive symptoms and health-related quality of life: The heart and soul study. JAMA 2003;290:215-21.
7. Rutledge T, Reis VA, Linke SE, Greenberg BH, Mills PJ. Depression in heart failure a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes. J Am Coll Cardiol 2006;48:1527-37.
8. Khattab K, Khattab AA, Ortak J, Richardt G, Bonnemeier H. Iyengar yoga increases cardiac parasympathetic nervous modulation among healthy yoga practitioners. Evid Based Complement Alternat Med 2007;4:511-7.
9. Lenfant C, Chobanian AV, Jones DW, Roccella EJ, Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Seventh report of the Joint National Committee on the prevention, detection, evaluation, and treatment of high blood pressure (JNC 7): Resetting the hypertension sails. Hypertension 2003;41:1178-9.
10. Whelton PK, Carey RM, Aronow WS, Casey DE Jr., Collins KJ, Dennison Himmelfarb C, *et al*. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: Executive summary: A report of the American College of Cardiology/American Heart Association Task force on clinical practice guidelines. Circulation 2018;138:e426-83.

11. Matthews KA, Katholi CR, McCreath H, Whooley MA, Williams DR, Zhu S, *et al.* Blood pressure reactivity to psychological stress predicts hypertension in the CARDIA study. Circulation 2004;110:74-8.
12. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, *et al.* 2020 International Society of Hypertension global hypertension practice guidelines. Hypertension 2020;75:1334-57.
13. Stone RA, DeLeo J. Psychotherapeutic control of hypertension. N Engl J Med 1976;294:80-4.
14. Bleich HL, Boro ES. Systemic hypertension and the relaxation response. N Engl J Med 1977;296:1152-6.
15. Hagins M, States R, Selfe T, Innes K. Effectiveness of yoga for hypertension: Systematic review and meta-analysis. Evid Based Complement Alternat Med 2013;2013:649836.
16. Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, *et al.* Blood pressure lowering for prevention of cardiovascular disease and death: A systematic review and meta-analysis. Lancet 2016;387:957-67.
17. Murugesan R, Govindarajulu N, Bera TK. Effect of selected yogic practices on the management of hypertension. Indian J Physiol Pharmacol 2000;44:207-10.
18. Boone JL. Stress and hypertension. Prim Care 1991;18:623-49.
19. Daimon M, Kamba A, Murakami H, Takahashi K, Otaka H, Makita K, *et al.* Association between pituitary-adrenal axis dominance over the renin-angiotensin-aldosterone system and hypertension. J Clin Endocrinol Metab 2016;101:889-97.
20. Streeter CC, Gerbarg PL, Saper RB, Ciraulo DA, Brown RP. Effects of yoga on the autonomic nervous system, gamma-aminobutyric-acid, and allostasis in epilepsy, depression, and post-traumatic stress disorder. Med Hypotheses 2012;78:571-9.
21. Kamei T, Toriumi Y, Kimura H, Ohno S, Kumano H, Kimura K. Decrease in serum cortisol during yoga exercise is correlated with alpha wave activation. Percept Mot Skills 2000;90:1027-32.
22. Afonso RF, Balardin JB, Lazar S, Sato JR, Igarashi N, Santaella DF, *et al.* Greater cortical thickness in elderly female yoga practitioners-a cross-sectional study. Front Aging Neurosci 2017;9:201.
23. Gothe NP, Hayes JM, Temali C, Damoiseaux JS. Differences in brain structure and function among yoga practitioners and controls. Front Integr Neurosci 2018;12:26.
24. Selvamurthy W, Sridharan K, Ray US, Tiwary RS, Hegde KS, Radhakrishan U, *et al*. A new physiological approach to control essential hypertension. Indian J Physiol Pharmacol 1998;42:205-13.
25. Christa E, Srivastava P, Chandran DS, Jaryal AK, Yadav RK, Roy A, *et al.* Effect of yoga based cardiac rehabilitation on blood pressure variability and baroreflex sensitivity: RCT in patients post MI. Appl Psychophysiol Biofeedback 2023;48:1-15.
26. Schmidt T, Wijga A, Von Zur Mühlen A, Brabant G, Wagner TO. Changes in cardiovascular risk factors and hormones during a comprehensive residential three month Kriya yoga training and vegetarian nutrition. Acta Physiol Scand Suppl 1997;640:158-62.
27. Ceriello A. Possible role of oxidative stress in the pathogenesis of hypertension. Diabetes Care 2008;31 Suppl 2:S181-4.
28. Briones AM, Touyz RM. Oxidative stress and hypertension: Current concepts. Curr Hypertens Rep 2010;12:135-42.
29. Patil SG, Dhanakshirur GB, Aithala MR, Naregal G, Das KK. Effect of yoga on oxidative stress in elderly with grade-I hypertension: A randomized controlled study. J Clin Diagn Res 2014;8:C04-7.
30. Ornish D, Scherwitz LW, Billings JH, Brown SE, Gould KL, Merritt TA, *et al.* Intensive lifestyle changes for reversal of coronary heart disease. JAMA 1998;280:2001-7.
31. Manchanda SC, Narang R, Reddy KS, Sachdeva U, Prabhakaran D, Dharmanand S, *et al.* Retardation of coronary atherosclerosis with yoga lifestyle intervention. J Assoc Physicians India 2000;48:687-94.
32. Yogendra J, Yogendra HJ, Ambardekar S, Lele RD, Shetty S, Dave M, *et al.* Beneficial effects of yoga lifestyle on reversibility of ischaemic heart disease: Caring heart project of International Board of Yoga. J Assoc Physicians India 2004;52:283-9.
33. Prabhakaran D, Chandrasekaran AM, Singh K, Mohan B, Chattopadhyay K, Chadha DS, *et al.* Yoga-based cardiac rehabilitation after acute myocardial infarction: A randomized trial. J Am Coll Cardiol 2020;75:1551-61.
34. Tillin T, Tuson C, Sowa B, Chattopadhyay K, Sattar N, Welsh P, *et al.* Yoga and Cardiovascular Health Trial (YACHT): A UK-based randomised mechanistic study of a yoga intervention plus usual care versus usual care alone following an acute coronary event. BMJ Open 2019;9:e030119.
35. Amaravathi E, Ramarao NH, Raghuram N, Pradhan B. Yoga-based postoperative cardiac rehabilitation program for improving quality of life and stress levels: Fifth-year follow-up through a randomized controlled trial. Int J Yoga 2018;11:44-52.
36. Li J, Gao X, Hao X, Kantas D, Mohamed EA, Zheng X, *et al.* Yoga for secondary prevention of coronary heart disease: A systematic review and meta-analysis. Complement Ther Med 2021;57:102643.
37. Fields JZ, Walton KG, Schneider RH, Nidich S, Pomerantz R, Suchdev P, *et al.* Effect of a multimodality natural medicine program on carotid atherosclerosis in older subjects: A pilot trial of Maharishi Vedic Medicine. Am J Cardiol 2002;89:952-8.
38. Manchanda SC, Mehrotra UC, Makhija A, Mohanty A, Dhawan S, *et al.* Reversal of early atherosclerosis in metabolic syndrome by yoga: A randomized controlled trial. J Yoga Phys Ther 2013;3:132.
39. Cheng TO. Effect of Tai Chi on endothelial function. Clin Cardiol 2007;30:150.
40. Patil SG, Edmin C, Chandrasekaran AM, Singh K, Patil S, Roy A, *et al*. Abstract 16321: Does yoga based cardiac rehabilitation (Yoga-CaRe) programme improve endothelial function and reduce oxidative stress in patients with acute myocardial infarction? Circulation 2020;142. [doi: 10.1161/circ.142.suppl_3.16321].
41. Khurshid S, Choi SH, Weng LC, Wang EY, Trinquart L, Benjamin EJ, *et al.* Frequency of cardiac rhythm abnormalities in a half million adults. Circ Arrhythm Electrophysiol 2018;11:e006273.
42. Stewart S, Hart CL, Hole DJ, McMurray JJ. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. Am J Med 2002;113:359-64.
43. Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, Seward JB, *et al.* Coronary ischemic events after first atrial fibrillation: Risk and survival. Am J Med 2007;120:357-63.
44. Thrall G, Lane D, Carroll D, Lip GY. Quality of life in patients with atrial fibrillation: A systematic review. Am J Med 2006;119:448.e1-19.
45. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, *et al.* 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: Recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. Europace 2012;14:528-606.
46. Shusterman V, Lampert R. Role of stress in cardiac arrhythmias. J Atr Fibrillation 2013;5:834.
47. Lampert R, Jamner L, Burg M, Dziura J, Brandt C, Liu H, *et al.*

Triggering of symptomatic atrial fibrillation by negative emotion. J Am Coll Cardiol 2014;64:1533-4.
48. Lakkireddy D, Atkins D, Pillarisetti J, Ryschon K, Bommana S, Drisko J, *et al.* Effect of yoga on arrhythmia burden, anxiety, depression, and quality of life in paroxysmal atrial fibrillation: The yoga my heart study. J Am Coll Cardiol 2013;61:1177-82.
49. Sharma G, Mooventhan A, Naik G, Nivethitha L. A review on role of yoga in the management of patients with cardiac arrhythmias. Int J Yoga 2021;14:26-35.
50. Mukharji J, Rude RE, Poole WK, Gustafson N, Thomas LJ Jr., Strauss HW, *et al.* Risk factors for sudden death after acute myocardial infarction: Two-year follow-up. Am J Cardiol 1984;54:31-6.
51. Kostis JB, Byington R, Friedman LM, Goldstein S, Furberg C. Prognostic significance of ventricular ectopic activity in survivors of acute myocardial infarction. J Am Coll Cardiol 1987;10:231-42.
52. Saxon LA, Bristow MR, Boehmer J, Krueger S, Kass DA, De Marco T, *et al.* Predictors of sudden cardiac death and appropriate shock in the comparison of medical therapy, pacing, and defibrillation in heart failure (COMPANION) trial. Circulation 2006;114:2766-72.
53. Myerburg RJ, Kessler KM, Castellanos A. Sudden cardiac death: Epidemiology, transient risk, and intervention assessment. Ann Intern Med 1993;119:1187-97.
54. Myerburg RJ, Interian A Jr., Mitrani RM, Kessler KM, Castellanos A. Frequency of sudden cardiac death and profiles of risk. Am J Cardiol 1997;80:10F-9F.
55. Hallstrom AP, Eisenberg MS, Bergner L. The persistence of ventricular fibrillation and its implication for evaluating EMS. Emerg Health Serv Q 1982;1:41-9.
56. Dabhade AM, Pawar BH, Ghunage MS, Ghunage VM. Effect of pranayama (breathing exercise) on arrhythmias in the human heart. Explore (NY) 2012;8:12-5.
57. Prakash ES, Ravindra PN, Madanmohan, Anilkumar R, Balachander J. Effect of deep breathing at six breaths per minute on the frequency of premature ventricular complexes. Int J Cardiol 2006;111:450-2.
58. Malik M, Camm AJ. Heart rate variability. Clin Cardiol 1990;13:570-6.
59. Phadumdeo VM, Weinberg SH. Heart rate variability alters cardiac repolarization and electromechanical dynamics. J Theor Biol 2018;442:31-43.
60. Nolan J, Batin PD, Andrews R, Lindsay SJ, Brooksby P, Mullen M, *et al.* Prospective study of heart rate variability and mortality in chronic heart failure: Results of the United Kingdom heart failure evaluation and assessment of risk trial (UK-heart). Circulation 1998;98:1510-6.
61. Zou L, Sasaki JE, Wei GX, Huang T, Yeung AS, Neto OB, *et al.* Effects of mind ‑ body exercises (Tai Chi/yoga) on heart rate variability parameters and perceived stress: A systematic review with meta-analysis of randomized controlled trials. J Clin Med 2018;7:404.
62. Ghati N, Killa AK, Sharma G, Karunakaran B, Agarwal A, Mohanty S, *et al*. A randomized trial of the immediate effect of bee-humming breathing exercise on blood pressure and heart rate variability in patients with essential hypertension. Explore (NY) 2021;17:312-9.
63. Bartoletti A, Fabiani P, Bagnoli L, Cappelletti C, Cappellini M, Nappini G, *et al.* Physical injuries caused by a transient loss of consciousness: Main clinical characteristics of patients and diagnostic contribution of carotid sinus massage. Eur Heart J 2008;29:618-24.
64. van Dijk N, Sprangers MA, Boer KR, Colman N, Wieling W, Linzer M. Quality of life within one year following presentation after transient loss of consciousness. Am J Cardiol 2007;100:672-6.
65. Gunda S, Kanmanthareddy A, Atkins D, Bommana S, Pimentel R, Drisko J, *et al.* Role of yoga as an adjunctive therapy in patients with neurocardiogenic syncope: A pilot study. J Interv Card Electrophysiol 2015;43:105-10.
66. Shenthar J, Gangwar RS, Banavalikar B, Benditt DG, Lakkireddy D, Padmanabhan D. A randomized study of yoga therapy for the prevention of recurrent reflex vasovagal syncope. Europace 2021;23:1479-86.
67. Brown RP, Gerbarg PL. Yoga breathing, meditation, and longevity. Ann N Y Acad Sci 2009;1172:54-62.
68. Nivethitha L, Mooventhan A, Manjunath NK. Effects of various prāṇāyāma on cardiovascular and autonomic variables. Anc Sci Life 2016;36:72-7.
69. Telles S, Nagarathna R, Nagendra HR. Autonomic changes during “OM” meditation. Indian J Physiol Pharmacol 1995;39:418-20.
70. Severino P, Mariani MV, Maraone A, Piro A, Ceccacci A, Tarsitani L, *et al*. Triggers for Atrial Fibrillation: The Role of Anxiety. Cardiol Res Pract 2019;2019:1208505.
71. Ashraf A. Anxiety and atrial fibrillation: An interesting bidirectional association. Curr Trend Cardiol 2017;1:15-8.
72. Szardien S, Möllmann H, Willmer M, Akashi YJ, Hamm CW, Nef HM. Mechanisms of stress (takotsubo) cardiomyopathy. Heart Fail Clin 2013;9:197-205, ix.
73. Mahida S, Sacher F, Derval N, Berte B, Yamashita S, Hooks D, *et al.* Science linking pulmonary veins and atrial fibrillation. Arrhythm Electrophysiol Rev 2015;4:40-3.
74. Han J, Garciadejalon P, Moe GK. Adrenergic effects on ventricular vulnerability. Circ Res 1964;14:516-24.
75. Shen MJ, Fishbein MC, Chen LS, Lin SF, Chen PS. In: Cardiac Electrophysiology: From Cell to Bedside. Zipes DP, Jalife J, Stevenson WG, editors. In: Neural activity and atrial tachyarrhythmias; 7th ed. New York: Elsevier; 2018. p. 375-86.
76. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: A systematic analysis for the global burden of disease study 2013. Lancet 2015;385:117-71.
77. Sayer G, Bhat G. The renin-angiotensin-aldosterone system and heart failure. Cardiol Clin 2014;32:21-32, vii.
78. Piña IL, Apstein CS, Balady GJ, Belardinelli R, Chaitman BR, Duscha BD, *et al.* Exercise and heart failure: A statement from the American Heart Association Committee on exercise, rehabilitation, and prevention. Circulation 2003;107:1210-25.
79. Piepoli MF, Corrà U, Benzer W, Bjarnason-Wehrens B, Dendale P, Gaita D, *et al.* Secondary prevention through cardiac rehabilitation: From knowledge to implementation. A position paper from the cardiac rehabilitation section of the European Association of Cardiovascular Prevention and Rehabilitation. Eur J Cardiovasc Prev Rehabil 2010;17:1-17.
80. Pullen PR, Nagamia SH, Mehta PK, Thompson WR, Benardot D, Hammoud R, *et al.* Effects of yoga on inflammation and exercise capacity in patients with chronic heart failure. J Card Fail 2008;14:407-13.
81. Kubo A, Hung YY, Ritterman J. Yoga for heart failure patients: A feasibility pilot study with a multiethnic population. Int J Yoga Therap 2011;(21):77-83.
82. Krishna BH, Pal P, Pal GK, Balachander J, Jayasettiaseelon E, Sreekanth Y, *et al.* Effect of yoga therapy on heart rate, blood pressure and cardiac autonomic function in heart failure. J Clin

Diagn Res 2014;8:14-6.
83. Krishna BH, Pal P, Pal G, Balachander J, Jayasettiaseelon E, Sreekanth Y, *et al*. A randomized controlled trial to study the effect of yoga therapy on cardiac function and N terminal Pro BNP in heart failure. Integr Med Insights 2014;9:1-6.
84. Agostoni P, Bussotti M, Cattadori G, Margutti E, Contini M, Muratori M, *et al.* Gas diffusion and alveolar-capillary unit in chronic heart failure. Eur Heart J 2006;27:2538-43.
85. Yadav A, Singh S, Singh K, Pai P. Effect of yoga regimen on lung functions including diffusion capacity in coronary artery disease patients: A randomized controlled study. Int J Yoga 2015;8:62-7.
86. Sigurdsson A, Swedberg K. The role of neurohormonal activation in chronic heart failure and postmyocardial infarction. Am Heart J 1996;132:229-34.
87. Abdulla J, Pogue J, Abildstrøm SZ, Køber L, Christensen E, Pfeffer MA, *et al.* Effect of angiotensin-converting enzyme inhibition on functional class in patients with left ventricular systolic dysfunction – A meta-analysis. Eur J Heart Fail 2006;8:90-6.
88. Abdulla J, Køber L, Christensen E, Torp-Pedersen C. Effect of beta-blocker therapy on functional status in patients with heart failure – A meta-analysis. Eur J Heart Fail 2006;8:522-31.
89. Pullen PR, Thompson WR, Benardot D, Brandon LJ, Mehta PK, Rifai L, *et al.* Benefits of yoga for African American heart failure patients. Med Sci Sports Exerc 2010;42:651-7.
90. Tran MD, Holly RG, Lashbrook J, Amsterdam EA. Effects of Hatha yoga practice on the health-related aspects of physical fitness. Prev Cardiol 2001;4:165-70.
91. Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. Circulation 2002;105:1135-43.
92. Pitsavos C, Panagiotakos DB, Papageorgiou C, Tsetsekou E, Soldatos C, Stefanadis C. Anxiety in relation to inflammation and coagulation markers, among healthy adults: The ATTICA study. Atherosclerosis 2006;185:320-6.
93. Chohan IS, Nayar HS, Thomas P, Geetha NS. Influence of yoga on blood coagulation. Thromb Haemost 1984;51:196-7.
94. Gordon LA, Morrison EY, McGrowder DA, Young R, Fraser YT, Zamora EM, *et al.* Effect of exercise therapy on lipid profile and oxidative stress indicators in patients with type 2 diabetes. BMC Complement Altern Med 2008;8:21.
95. Damodaran A, Malathi A, Patil N, Shah N, Suryavansihi, Marathe S. Therapeutic potential of yoga practices in modifying cardiovascular risk profile in middle aged men and women. J Assoc Physicians India 2002;50:633-40.
96. Mahajan AS, Reddy KS, Sachdeva U. Lipid profile of coronary risk subjects following yogic lifestyle intervention. Indian Heart J 1999;51:37-40.
97. Kiecolt-Glaser JK, Christian L, Preston H, Houts CR, Malarkey WB, Emery CF, *et al.* Stress, inflammation, and yoga practice. Psychosom Med 2010;72:113-21.
98. Riley KE, Park CL. How does yoga reduce stress? A systematic review of mechanisms of change and guide to future inquiry. Health Psychol Rev 2015;9:379-96.
99. Buric I, Farias M, Jong J, Mee C, Brazil IA. What is the molecular signature of mind-body interventions? A systematic review of gene expression changes induced by meditation and related practices. Front Immunol 2017;8:670.
100. Cole SW. The conserved transcriptional response to adversity. Curr Opin Behav Sci 2019;28:31-7.
101. Simons RL, Lei MK, Beach SR, Barr AB, Cutrona CE, Gibbons FX, *et al.* An index of the ratio of inflammatory to antiviral cell types mediates the effects of social adversity and age on chronic illness. Soc Sci Med 2017;185:158-65.
102. Harkess KN, Ryan J, Delfabbro PH, Cohen-Woods S. Preliminary indications of the effect of a brief yoga intervention on markers of inflammation and DNA methylation in chronically stressed women. Transl Psychiatry 2016;6:e965.
103. Bock BC, Thind H, Fava JL, Dunsiger S, Guthrie KM, Stroud L, *et al.* Feasibility of yoga as a complementary therapy for patients with type 2 diabetes: The healthy active and in control (HA1C) study. Complement Ther Med 2019;42:125-31.
104. Thind H, Lantini R, Balletto BL, Donahue ML, Salmoirago-Blotcher E, Bock BC, *et al.* The effects of yoga among adults with type 2 diabetes: A systematic review and meta-analysis. Prev Med 2017;105:116-26.
105. Khatri D, Mathur KC, Gahlot S, Jain S, Agrawal RP. Effects of yoga and meditation on clinical and biochemical parameters of metabolic syndrome. Diabetes Res Clin Pract 2007;78:e9-10.
106. Chu P, Gotink RA, Yeh GY, Goldie SJ, Hunink MG. The effectiveness of yoga in modifying risk factors for cardiovascular disease and metabolic syndrome: A systematic review and meta-analysis of randomized controlled trials. Eur J Prev Cardiol 2016;23:291-307.
107. Malhotra V, Singh S, Tandon OP, Sharma SB. The beneficial effect of yoga in diabetes. Nepal Med Coll J 2005;7:145-7.
108. Thangasami SR, Chandani AL, Thangasami S. Emphasis of yoga in the management of diabetes. J Diabetes Metab 2015;6:613.
109. Manjunatha S, Vempati RP, Ghosh D, Bijlani RL. An investigation into the acute and long-term effects of selected yogic postures on fasting and postprandial glycemia and insulinemia in healthy young subjects. Indian J Physiol Pharmacol 2005;49:319-24.
110. Singh RB, Wilczynska-Kwiatek A, Fedacko J, Pella D, De Meester F. Pranayama: The power of breath. Int J Disabil Hum Dev 2009;8:141-53.
111. Innes KE, Bourguignon C, Taylor AG. Risk indices associated with the insulin resistance syndrome, cardiovascular disease, and possible protection with yoga: A systematic review. J Am Board Fam Pract 2005;18:491-519.
112. Cramer H, Lauche R, Langhorst J, Dobos G. Is one yoga style better than another? A systematic review of associations of yoga style and conclusions in randomized yoga trials. Complement Ther Med 2016;25:178-87.
113. Braunwald E, Epstein SE, Glick G, Wechsler AS, Braunwald NS. Relief of angina pectoris by electrical stimulation of the carotid-sinus nerves. N Engl J Med 1967;277:1278-83.
114. Scheffers IJ, Kroon AA, Schmidli J, Jordan J, Tordoir JJ, Mohaupt MG, *et al.* Novel baroreflex activation therapy in resistant hypertension: Results of a European multi-center feasibility study. J Am Coll Cardiol 2010;56:1254-8.
115. Schwartz PJ, De Ferrari GM, Sanzo A, Landolina M, Rordorf R, Raineri C, *et al.* Long term vagal stimulation in patients with advanced heart failure: First experience in man. Eur J Heart Fail 2008;10:884-91.
116. Premchand RK, Sharma K, Mittal S, Monteiro R, Dixit S, Libbus I, *et al.* Autonomic regulation therapy via left or right cervical vagus nerve stimulation in patients with chronic heart failure: Results of the ANTHEM-HF trial. J Card Fail 2014;20:808-16.
117. Sheng X, Scherlag BJ, Yu L, Li S, Ali R, Zhang Y, *et al.* Prevention and reversal of atrial fibrillation inducibility and autonomic remodeling by low-level vagosympathetic nerve stimulation. J Am Coll Cardiol 2011;57:563-71.
118. Clancy JA, Mary DA, Witte KK, Greenwood JP, Deuchars SA, Deuchars J. Non-invasive vagus nerve stimulation in healthy humans reduces sympathetic nerve activity. Brain Stimul 2014;7:871-7.