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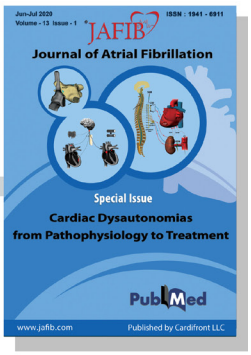

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Impact of Yoga on Cardiac Autonomic Function and Arrhythmias

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Abstract

With the expanding integration of complementary and alternative medicine (CAM) practices in conjunction with modern medicine, yoga has quickly risen to being one of the most common CAM practices across the world. Despite widespread use of yoga, limited studies are available, particularly in the setting of dysrhythmia. Preliminary studies demonstrate promising results from integration of yoga as an adjunct to medical therapy for management of dysrhythmias. In this review, we discuss the role of autonomic nervous system in cardiac arrhythmia,interaction of yoga with autonomic tone and its subsequent impact on these disease states. The role of yoga in specific disease states, and potential future direction for studies assessing the role of yoga in dysrhythmia.

Introduction

Yoga is an ancient practice utilizing diverse postures and movements in conjunction with breathing methods geared towards facilitating a meditative state. While the practice of yoga is speculated to have existed since the 5000 BC, only more recently has clinical application of yoga and other similar alternative practices been evaluated within the context of modern medicine. Yoga is the most common alternative practice in the United States (USA) with an estimated 20.4 million people currently practicing - a dramatic increase (29%) from 2008 where 15.8 million people practiced[1]. There is growing body of evidence that, shows the beneficial effects of yoga as an adjunct to conventional treatments for various disease conditions including – chronic pain, orthopedic issues, heart failure, atrial fibrillation and many more. Autonomic nervous system (ANS) plays an important role in the initiation and maintenance of atrial arrhythmias. In this manuscript, we try to shed some light on the unique interaction between cardiac autonomic system and yoga.

Key Words

Dysrhythmia, Atrial Fibrillation, Ventricular Arrhythmia, Neurocardiogenic Syncope, Yoga

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Fundamentals of Yoga

Yoga is a philosophy and a way of life formalized by Patanjali 2000 years ago. This practice aimed to balance mind, body and spirit leading to calmness of mind and alleviation of psychological distress using eight foundational principles: yama(morality/restraint), niyama (duties), asana (posture – examples in Figure 1), pranayama (breathing technique), pratyahara(sense withdrawal), dharana (focused concentration),dhyana(meditative absorption), samadhi(enlightenment). Since development, yoga is broadly categorized into four major types with multiple styles. The four major traditional types of yoga include: Bhakti, Gnana (pronounced as ñana), Karma, and Kriya (with Hatha, Tantra, and Kundalini yoga subtypes). There are many particular styles of yoga practice as well (Table 1) [2].

It is based on the premise that, a central consciousness regulates the bodily function through flow of energy through Chakras distributed along the spinal column inwards and outwards. A Chakra

Table 1: Yoga Types and Styles

Yoga Types	Styles
Bhakti	Iyengar
Gnana	Vinyasa
Karma	Hot
Kriya (Hatha, Tantra, and Kundalini subtypes)	Ashtanga
	Sivananda
	Yin
	Restorative
	Anusara
	Prenatal
	Jivamukti
	Bikram

is a powerhouse in the way it generates and stores energy, with the energy from cosmos pulled in more strongly at these points. The nadis – Ida (sympathetic) and Pingala (parasympathetic) run along the spinal column in a curved path and cross one another several times joining the Shushumna (central nervous system) at the top of the spinal column. At the points of intersection, they form strong energy centers known as chakras (spinal plexi) .(Figure -1).

Simply knowing the many different styles of yoga, one can begin to appreciate the difficulty in evaluating such a practice with uniformity. A major limitation to consider within the growing body of yoga research is the wide variability in what is considered yoga. As a result of heterogeneity (such as differences in yoga style, length of study, amount of time yoga is used, baseline population difference), identification of potential mechanisms of outcome improvement and ideal patient population can potentially be problematic as studies would ideally have replicable and cohesive findings that can be applied incrementally. Consequently, it can be difficult to make any generalizable statements about yoga and major studies should be individually assessed [3]. Among available evidence for styles of yoga studied, no individual practice has been found to demonstrate significant superiority [4].

Impact of yoga on autonomic function and neurohormonal modulation:

Yoga offers many beneficial effects on autonomic nervous system through modulation of rate, depth and pattern of breathing [5]. Previously studies have shown that, yogic breathing can exert its positive effects through increasing heart rate variability, improving sympatho-vagal balance and promoting stress resilience [6-8]. It was hypothesized that, yogic breathing causes activation of stretch receptors in the respiratory system to relay information through vagal afferents to central nervous system (CNS) areas to positively influence cognition, emotion, perception, behavior and somatic expression[6, 7]. It is believed that, yoga practices modulate the stress related imbalances through increasing parasympathetic system, and γ-aminobutyric acid (GABA) system while decreasing hypothalamic – pituitary –adrenal axis [5]. Additionally, yoga exercise was shown

Figure 1: Examples of Yoga Postures (Asanas)

Top row (left to right): Downward Dog, Mountain, Plough, Goddess, Tree Middle row: Lord of Dance, Plank, Lotus, Side Plank, Scorpion Bottom Row: Crescent, Wheel, Dancing Shiva, Lord of Fishes, Sundial

to have positive role in reducing stress, anxiety and depression in young women and can be utilized as a complimentary medicine [9]. The other positive effects of yoga exercise includes decrease in heart rate and blood pressure (systolic, diastolic and mean arterial) [10]. The ancient Om mantra which is routinely used with yoga is associated with decreased vagal tone, physiological relaxation and limbic system deactivation [11, 12]. Yoga therapy has been demonstrated to reduce the systemic inflammatory response (Cortisol, CRP and IL-6), attenuate endothelial dysfunction and allosteric load [13, 14].

Patients with 4 months of transcendental meditation therapy demonstrated attenuation of levels of stress hormones such as cortisol, testosterone, growth hormone GH and thyroid stimulating hormone (TSH) as compared to control group emphasizing its importance in reversing the effects of chronic stress that can contribute to disease [15]. In a randomized control trial, yoga therapy results in improvement of parameters of heart rate variability (HRV) especially those related to vagal tone such as SDNNi and rMSSD [16]. Deep breathing exercises and relaxation leads to 50% reduction in premature ventricular contractions (PVC) burden through effects on cardiac autonomous system (ANS) and purkinje system along with QT dispersion [17]. In patients with neurocardiogenic syncope, yoga therapy has been

Table 2: General Physiologic Mechanisms of Major Yoga Components

Posture (*Asana*)	Breath Control (*Pranayama*)	Meditation (*Dhyana*)
Aerobic Exercise • Autonomic Modulation • Underlying risk factor improvement (obesity, blood pressure control etc.) • Psychological Stress Reduction	Pulmonary Stretch • Autonomic modulation • Heart Rate/Blood Pressure control	Psychological Stress Reduction • Limbic/Autonomic attenuation
Isometric Resistance • Muscle Strength • Psychological Stress Reduction	Psychological Stress Reduction • Limbic/Autonomic attenuation • HPA Modulation	Improved Self Control • Urge improvement and reduction of preventable risk factors

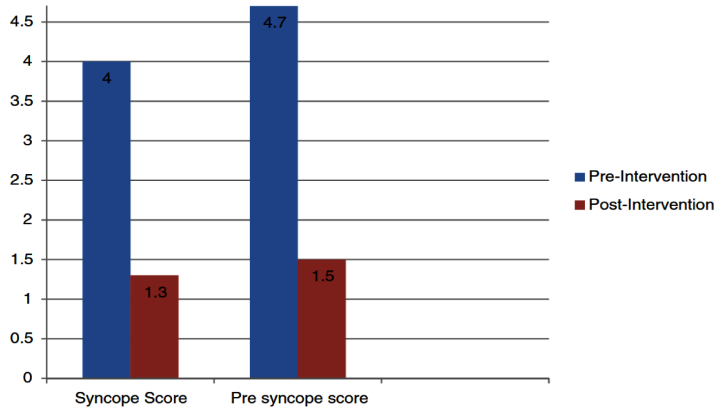

Figure 2: Impact on of Yoga on Syncopal and Presyncopal Episodes

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shown to improve the symptoms of syncope and presyncope [18]. In the patients with cardiac arrhythmias, pranayama yoga therapy has been shown to reduce the ventricular repolarization dispersion thereby lowering the risk of developing malignant ventricular arrhythmias and sudden cardiac death [19]. In heart failure patients, yoga therapy resulted in reduction in heart rate and blood pressure due to improved HRV, increased vagal tone and decreased sympathetic tone [20].

Emotional stress and cardiac Arrhythmias

It is widely believed that, different emotions in humans are processed in different parts of forebrain. Positive emotions are processed in the left hemisphere whereas negative emotions were processed in the right hemisphere. Accordingly, positive emotions activate sympathetic neurons from the right hemisphere whereas negative emotions activate parasympathetic neurons from the left hemisphere. Right sided nerves innervate anterior aspect (right ventricle) whereas left sided nerves innervate postero-lateral aspect (left ventricle) resulting in lateralized innervation of heart. This lateralized emotional processing in the cortex along with lateralized innervation of the heart results in asymmetrical stimulation of heart, generation of repolarization heterogenecity, and electrical instability resulting in facilitation of reentrant arrhythmias [21-23]

Psychiatric disorders such as anxiety, depression and emotional stress were considered as common triggering points for cardiac arrhythmias such as atrial fibrillation (AF). Following an episode of anger or negative emotions, the likelihood of developing AF will be increased to 5 fold whereas risk is decreased with episode of happiness [24, 25]. It is important to note that, anxiety associated with impatience, competitiveness and job involvement significantly increases the risk of developing AF [24, 26]. There is no direct relationship between emotional disorders and cardiac arrhythmias, but researchers proposed various pathological mechanisms thereby strengthening the causative relationship between these two clinical entities. Emotional stress and anxiety can lead to pathological consequences on neuroendocrine, coagulative, microcirculatory, immune systems ultimately resulting in cardiac arrhythmias [27].

ATTICA study had demonstrated that, anxiety is associated with upreglation of inflammatory markers such as C-reactive protein, interleukin-6, homocycteine and fibrinogen levels [28]. Accordingly, systemic inflammatory response and hypercoagulation state associated with anxiety can predispose to development of cardiac arrhythmias [28]. Moreover, inflammatory state of anxiety can attributed to excess activation of hypothalamic-pituitary adrenal axis with cortisol overproduction and associated imbalance of dopaminergic, serotoninergic and non-adrenergic neurons [29]. Additionally, activation of sympathetic system with catecholamine overload can lead to extracellular matrix production, upregulation of collagen production, increased transforming growth factor beta 1 or TGF-β1, mononuclear infiltration, and reactive oxygen species (ROS) production resulting in negative atrial remodeling and atrial fibrosis [27, 30-35]. Lastly, anxiety can lead to activation of rennin angiotensin system (RAS) and over production of angiotension II leading to atrial fibrosis, left ventricular hypertrophy, and increased atrial pressure/stretch which ultimately results in AF [27, 35]. Emotional disorders commonly activate the autonomous ganglia to initiate ectopic impulses in myocardial cells in pulmonary veins near their connection with left atrium and predispose to development of AF[36].

Although most studies are small with limitations making it difficult to draw definitive conclusions given data quality, evidence exists to suggest that regular practice of yoga results in increased resting vagal tone. This conclusion is discerned based on markers of autonomic activity such as heart rate (HR)/HRV, Baroreceptor sensitivity, cognitive ability and emotional regulation. In certain disease states (such as diabetes, psychiatric conditions, pain and hypertension), yoga has demonstrated some benefit as an adjunct therapy [37-42]. Despite individual study findings, definitive conclusions are controversial and will require further investigation [43, 44].

Autonomic etiology of dysrhythmias and impact of YogaIntroduction

Reflex Syncope

Syncope is loss of consciousness resulting from transient global cerebral hypo-perfusion typically due to neuroendocrine, orthostatic, arrhythmogenic and structural cardiopulmonary etiology. Reflex syncope collectively describes: neurocardiogenic (vasovagal) syncope, situational syncope (cough, micturition etc.), and carotid sinus syndrome (CSS) [45-47].

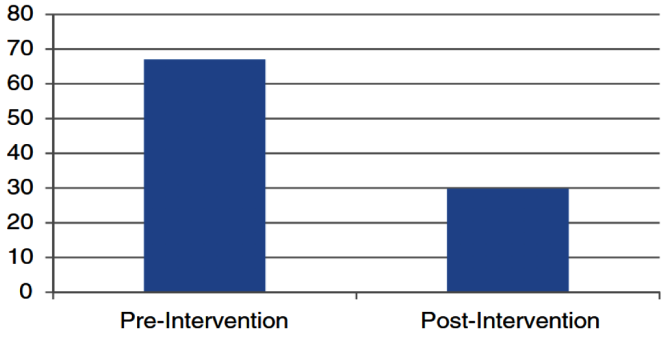

Figure 3: Impact on of Yoga on Syncopal Functional Status Questionnaire Score (SFSQS)

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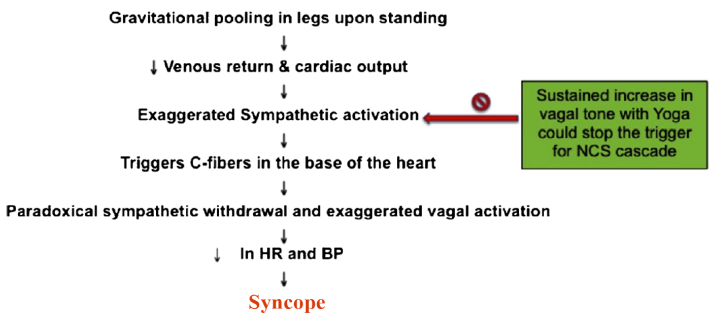

Figure 4: Role of Yoga in Neurocardiogenic Syncope

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The most common type of reflex syncope is neuro-cardiogenic and is commonly associated with reduced blood volume, dehydration, and elevated sympathetic tone [48, 49]. Ventricular stimulation in response to excess catecholamines triggers ventricular mechanoreceptors carrying signal to the medulla via the vagus nerve. The resulting efferent response creates a paradoxical attenuation in sympathetic tone with concurrent heightening of vagal tone. The consequence of this Bezold-Jarisch reflex is hypotension, and bradycardia (due to SA the sinoatrial impulse suppression in conjunction with reduction in AV the atrioventricular nodal conduction). Conservative measures consist of: trigger (prolonged standing, dehydration, temperature extreme) avoidance, counterpressure maneuvers (handgrip, squat, leg crossing), adequate hydration, salt intake, compression stockings, and tilt training[46, 47, 50-54]. Potential medications used include beta blockers, midodrine, fludrocortisone, selective serotonin reuptake inhibitors (SSRIs), and ivabradine. More invasive procedures with limited evidence include ganglionated plexus cardio-neuroablation and pacemaker implantation [55].

In 2015, Gunda et. al [42]. published a pilot study on the role of yoga as an adjunct therapy for neuro-cardiogenic syncope. This was a multicenter observational study which enrolled 44 patients with neuro-cardiogenic syncope in 2 arms -- a control arm (23 patients) and an intervention yoga arm (21 patients). The control arm was monitored via log of syncopal and presyncopal episodes experienced over a six-month period. The intervention group had a 60-minute yoga video they were asked to participate in 3 times weekly for 3 months. All patients had a baseline history and physical examination, syncope functional questionnaire score (SFSQS), and head up tilt test (HUTT). At the end of the study, only the intervention group had a repeat HUTT and SFSQS. A positive HUTT was defined by the presence of bradycardia (HR under 40 for > 10 seconds or asystole for >3 seconds) and/or vasodepressor response (symptomatic hypotension or systolic blood pressure (BP) reduction below 60 mmHg). The study found a significant difference between the control and intervention group in mean syncopal episodes (4.0 + 1.0 vs. 1.3 + 0.7, $p < 0.001$), mean pre-syncopal episodes (4.7 + 1.5 vs. 1.5 + 0.5, $p < 0.001$), and reduction in SFSQS (67 + 7.8 vs. 29.8 + 4.6, $p < 0.001$) (Figures 2 and 3). Additionally, within the intervention group it was noted that, all patients began with a positive HUTT but at the conclusion of the study, only 28% (6 patients) had a positive HUTT. Findings from the study demonstrate the clinical efficacy of yoga as an adjunct therapy in management of patients with neuro-cardiogenic syncope via accelerating blood volume return to the heart (similar to counter-pressure maneuvers previously mentioned) in conjunction with autonomic modulation (Figure 4) [18].

Atrial Fibrillation

AF has a well-established connection with the ANS. Heightened sympathetic tone with subsequent vagal overcompensation results in a milieu of shortened refractory period in conjunction with premature atrial beats, resulting in AF [56, 57]. Sympathetic activation can help propagate AF via beta-adrenergic receptor activation. The following vagal hyperactivity results in shortening of the refractory period as well as action potential duration [58]. This, in conjunction with more recent evidence suggesting involvement of local cardiac ANS, specifically the modulatory effect of ganglionic plexi (GP), represents the current model for the underlying mechanism of AF [59]. There is evidence to show that, in some paroxysms of AF there is a significant surge in sympathetic tone preceding an AF episode which is triggered by a sudden withdrawal of the same and increase in parasympathetic tone. These types of sudden variations in cardiac autonomic tone form the patho-physiologic platform for many other types of arrhythmia substrates as well.

In 2013, The YOGA My Heart Study by our group assessed the clinical impact of yoga in patients with atrial fibrillation [60]. The YOGA My Heart Study was a single center, self-controlled, cohort study conducted over a period of 6 months total (3 months with no yoga vs. 3 months with yoga). Baseline quality of life, depression and anxiety scores, hemodynamic parameters (HR and BP), and atrial fibrillation (AF) burden (using event monitor and self-reporting of symptoms) were used to evaluate at baseline (day 0), end of the control period (day 90) and end of the yoga intervention period (day 180). Patients were recommended to record at least one event on monitor per day even if asymptomatic. Yoga performed was structured Iyengar yoga occurring twice weekly with an instructor leading the class for approximately 60 minutes. Data from a total of 49 patients were used to assess comparative outcomes.

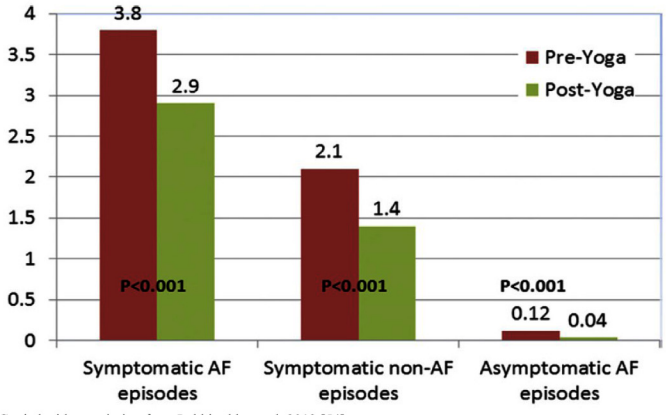

Figure 5: In all Categories, regular practice of yoga was found to improve outcomes

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Table 3: Physiologic Impact of Breath Control (Pranayama) Techniques

Slow Breathing			Fast Breathing		
Nadi Shodhana	***Savitri***	***Pranava***	***Kapalabhati***	***Bhastrika***	***Kukkuriya***
Psychological Stress Reduction	Psychological Stress Reduction	Psychological Stress Reduction	Psychological Stress Reduction	Psychological Stress Reduction	Psychological Stress Reduction
Variable effects		Decreased HR	Decreased Baroreflex Sensitivity	Decreased HRV	
		Decreased BP and PP	Decreased RR	Decreased BP	
		Increased Baroreflex Sensitivity	Increased SBP		
		Increased endogenous nitric oxide production			

HR: Heart Rate; BP: Blood Pressure; PP: Pulse Pressure; HRV: Heart Rate Variability
NadiShodhana: Alternate Nostril Breathing.
Savitri: Controlled, slow, deep breathing.
Pranava: Deep, meditative, slow breathing.
Kapalbhati: Passive inspiration with forceful expiration.
Bhastrika: Single nostril inspiration, breath holding and forced expiration using alternate nostril.
Kukkuriya: Fast mouth breathing.

Event monitor recorded episodes were categorized into symptomatic AF, symptomatic non-AF, and asymptomatic AF. In all categories, regular practice of yoga was found to improve outcomes (Shown in Figure 5):

· Reduction in mean number of symptomatic AF episodes: from 3.8+3 to 2.1+ 2.6 ($p < 0.001$).
· Reduction in mean number of symptomatic non-AF episodes: from 2.9+3.4 to 1.4+ 2.0 ($p < 0.001$).
· Reduction in mean number of asymptomatic AF episodes: from 0.12+0.44 to 0.04+ 0.20 ($p < 0.001$).

Of the patients with documented AF during the control phase, 22% did not have any observed episodes during the intervention phase. Aside from proof of concept regarding AF burden reduction, regular practice of yoga was demonstrated to reduce baseline heart rate as well as systolic and diastolic blood pressure. Other parameters measured including depression, anxiety, and quality of life scores improved as well. Notably, reduction in AF burden did not seem to correlate with change in hemodynamic parameters. The authors went to explain the improvement in depression, anxiety and quality of life by mentioning the effect of yoga on attenuation of stress response. They additionally hypothesized a plausible mechanism for AF prevention through regular practice of yoga: increased baseline parasympathetic tone, reduction in ANS fluctuations, and reduction in progression of AF through prevention or limiting of atrial remodeling [60].

Ventricular arrhythmia and sudden cardiac death

Within the heart, parasympathetic PANS and sympathetic SANS have a high degree of variability in distribution. Parasympathetic PANS has a much more focal spread than sympathetic SANS and is localized primarily in the sinoatrial (SA) node, the atrioventricular (AV) node and ganglionic plexi GPs embedded in atrial fat pads. Increased parasympathetic tone decreases rate of firing from the sinoatrial node SA node and the atrioventricular AV nodal conduction velocity. This same effect is very much limited within ventricular muscle where sympathetic innervation plays a primary role. Although it appears that SANS sympathetic and PANS parasympathetic systems have opposite function, it should be noted that SANS and PANS both systems work synchronously.

Myocardial infarction with resultant nerve and muscle necrosis creates a focus with a relative absence of sympathetic regulation - a functional denervation. In conjunction with surrounding tissue hypersensitivity, denervation (with resulting reduction in vagal tone) and tissue non-uniformity results in variable tissue refractory period resulting in ventricular ectopy.

Nerve sprouting in subsequent Wallerian degeneration is propagated by neural growth factor (NGF). This sprouting results in sympathetic hyperactivity - working in conjunction with factors mentioned above to enhance sympathetic SANS activation [61]. Enhanced SANS sympathetic activation is a known cause (based on animal models) for ventricular arrhythmia (VA) and sudden cardiac death (SCD) [62-64]. In chronic catecholamine elevation, a situation commonly observed in heart failure, sympathetic neural dysfunction is observed similar to denervation in myocardial infarction. As a result, management which entails mortality benefit in heart failure typically entails use of medication that attenuates sympathetic activation. Medications commonly used for this includes angiotensin-converting enzymeACE inhibitors, beta blockers and spironolactone [61]. More recently studies focusing on interventions geared towards sympathetic modulation have shown promising results on management of ventricular arrhythmiaVA [65].

In a similar way, the heightened parasympathetic tone which goes hand in hand with the sympathetic attenuation with regular practice of yoga may be helpful as an adjunctive therapy in such a setting. Of the three major components common in all styles of yoga (pranayama, asana, and dhyana), each component is thought to modulate arrhythmogenesis with slightly different mechanisms (Table 2) [3]. Among the three components, pranayama (breath control) has a significant body of supportive literature. Using different breath control techniques, variable impact on autonomic modulation can be achieved. Individual components of technique have been described including breath awareness (shown to independently reduce BP), slow breathing, and fast breathing (Table 3). Overall, pranayama is thought to reset ANS using slow deep breathing resulting in stretch induced inhibitory signaling. During inspiration, lung stretch activation of fibroblast slowly adapting stretch receptors results in inhibitory signaling and hyperpolarization of neural and non-neural tissue. This synchronizes neural elements of the heart, lungs, limbic system and cortex. The resulting autonomic modulation and decrease in metabolic activity suggests a parasympathetic augmentation. Another supported hypothesis suggests that, stretch receptor activation above tidal volume results in sympathetic tone withdrawal in peripheral blood vessels via Hering-Bruer reflex [66]. Future studies will need to better discern the benefit of yoga in the setting of

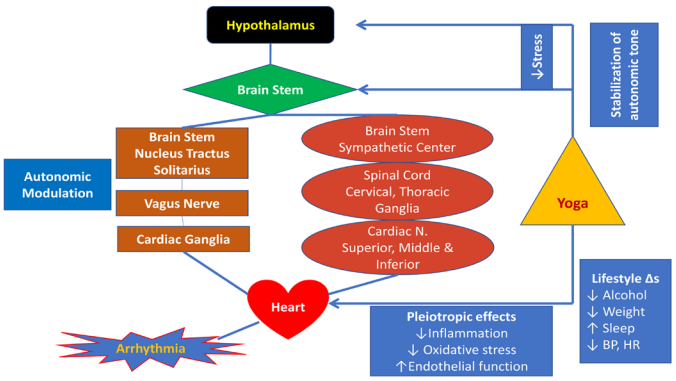

Figure 6: **Shows the multipronged impact of Yoga on human body and reduction of cardiac arrhythmias**

ventricular ectopy.

Yoga could potentially play a very important role in the prevention and treatment of cardiac arrhythmias. Through its pleiotrophic effect on improved endothelial function, reduction in oxidative stress and inflammation along with central and peripheral autonomic modulation combined with significant reduction in stress and lifestyle modification can translate into measurable reduction in arrhythmia burden and improvement in cardiac dysautonomia (Figure-6)

Conclusion and Future Directions

Yoga is an old complementary and alternative medicine (CAM) practice utilizing different movements, postures, and breathing techniques in conjunction with meditation. Early assessment of this practice as an adjunct to modern medical therapy has so far yielded promising results. The increase in vagal tone and reduction in autonomic fluctuation is the likely mechanism of how yoga reduces arrhythmia burden, improves hemodynamic parameters (such as resting HR and BP), and reduces symptoms. While future studies may attempt to differentiate styles of yoga or compare with similar CAM practices, yoga should be assessed in a variety of different dysrhythmias to improve our understanding of how and when this complementary practice should be used.

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