Unraveling the interplay between oxidative stress and vascular ageing with Yoga: A cross-sectional study

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ABSTRACT

**Background:** This research article explores the intricate relationship between oxidative stress vascular ageing and yoga. Oxidative stress, arising from an imbalance between reactive oxygen species (ROS) production and antioxidant defense mechanisms, plays a pivotal role in the physiological ageing process of blood vessels. Here, we dissect the molecular mechanisms underlying oxidative stress-induced vascular dysfunction, highlighting the involvement of key pathways such as endothelial dysfunction, inflammation, and vascular smooth muscle cell senescence. Furthermore, we discuss potential therapeutic strategies aimed at mitigating oxidative stress to prevent or delay vascular ageing and its associated pathologies with a special emphasis on yoga. The cross-sectional study aimed to explore the relationship between oxidative stress and vascular ageing and to dissect the effect of yoga in modulating this relationship.

**Materials and Methods:** 135 age-matched participants of both genders were investigated for their oxidative stress parameters after segregation based on their yoga practice.

**Results:** We found a significant (p<0.05) difference in the body mass index (BMI), and blood pressure (BP) phenotypes along with oxidative stress parameters in the participants performing regular yoga practice.

**Conclusion:** Our study found a beneficial effect of yoga on blood pressure and endothelial function which act by decreasing oxidative stress and delaying vascular ageing. Overall, this article underscores the importance of understanding the complex interplay between oxidative stress and vascular ageing for the development of novel interventions targeting age-related vascular diseases with special emphasis on yoga.

**Keywords:** Endothelial dysfunction, Functional age difference (FAD), Oxidative stress, Vascular age, Yoga.
INTRODUCTION

The ageing process is accompanied by a gradual decline in physiological function across various organ systems, including the cardiovascular system. Vascular ageing, characterized by structural and functional changes in blood vessels, is not only a hallmark of age-related cardiovascular diseases such as atherosclerosis, hypertension, and stroke etc. but an emerging field in the risk assessment of most of cardiovascular diseases [1]. While the mechanisms driving vascular ageing are multifaceted, growing evidence implicates oxidative stress as a key mediator in this process. Oxidative stress, resulting from an imbalance between the production of reactive oxygen species (ROS) and antioxidant defense mechanisms, exerts detrimental effects on the vasculature by promoting endothelial dysfunction, inflammation, and vascular smooth muscle cell (VSMC) senescence [2]. Understanding the intricate interplay between oxidative stress and vascular ageing is crucial for identifying novel therapeutic targets aimed at preserving vascular health in the ageing population as ageing of the vessels are modifiable [3]. Different types of yoga practices may play a significant role in the modulation of vascular architecture and hence may be involved in delaying the vascular age [4]. In this prospective cross-sectional study, we aimed to explore how oxidative stress and endothelial dysfunction are involved in the modulation of vascular ageing with a special emphasis on the relationships that can be interfered with yoga.

MATERIALS AND METHODS

Method of collection of data cum Study setting: This prospective cross-sectional study was conducted in the Centre for Yoga and Exercise Science, Department of Physiology, of Shri B M Patil Medical College Hospital and Research Centre of BLDE (Deemed to be University) after obtaining ethical clearance from the Institutional Ethical Committee (IEC/No-09/2021 Dated 22/01/2021) following which voluntary written informed consent was obtained from all the study participants. Age-matched 135 (75 males and 60 females) participants of both genders were segregated according to their history of yoga practice. Selection of all the participants was done through convenience sampling in which participants performing regular yoga practice for a minimum of more than three months were incorporated in group-1 while the participants with no yoga practice were included in group-2. Alcoholics, smokers, persons suffering from any chronic disease or persons taking regular medications which may alter the vascular architecture were excluded from our study.
Assessed parameters: The physiological parameters such as blood pressure phenotypes (systolic blood pressure, diastolic blood pressure, pulse pressure, mean arterial pressure), height, and weight were measured, and body mass index (BMI) was calculated following the latest World Health Organization (WHO) criteria. The vascular age was analyzed using a Periscope, an automated instrument that works on the oscillometric method [5]. After the physiological parameters were assessed, each of the participants was directed for 15 minutes rest following which the blood samples were collected for the analysis of serum malondialdehyde (MDA) and serum nitric oxide (NO) by using a UV spectrophotometer at 535 nm.

Statistical analysis: The data was obtained in a Microsoft Excel Sheet and the analysis was done using SPSS software Version 20. Unpaired Student’s Samples T’ test was applied to compare means and standard deviation. Post-analysis, the data was presented in mean ± standard deviation (SD) and the correlation was done using Spearman’s correlation. The presented data was considered significant if the p-value was found to be <0.05.

RESULTS

Table-1 shows the comparison of all the assessed parameters in both groups which show a significant increase in all the blood pressure phenotypes in group-2 than group-1. It also shows that group-2 participants have higher levels of malondialdehyde (MDA) and a lower value of nitric oxide (NO) than group-1 participants. We have also observed that the BMI in both groups has a statistically significant difference.

Table-2 shows the correlation of vascular age with all the other study parameters in both groups and the total study population. The findings from these correlations are inconclusive as the value of the correlation coefficient (r-value) of none of the correlations is more than 0.6 despite being statistically significant (p<0.05).

Table-3 shows the comparison of different age parameters. We have calculated the Functional Age Difference (FAD) by deducting the chronological age from the vascular age. It is clearly visible from our results that there is an average advancement of vascular age of more than 11 years in the participants who are not practicing yoga than the participants practicing yoga regularly for at least three months. This is evidence of yoga delaying vascular age or preventing the advancement in the ageing process of an individual.
Table-1: Comparison of all the study parameters assessed in both groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group-1 (n = 62)</th>
<th>Group-2 (n = 73)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>24.39 ± 2.99</td>
<td>27.12 ± 3.80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>125.42 ± 14.08</td>
<td>140.37 ± 14.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>75.76 ± 9.31</td>
<td>84.22 ± 9.29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td>49.66 ± 8.72</td>
<td>56.15 ± 10.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>92.31 ± 10.34</td>
<td>102.94 ± 10.34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MDA (μmol/L)</td>
<td>1.095 ± 0.37</td>
<td>1.622 ± 0.53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NO (μmol/L)</td>
<td>6.989 ± 1.88</td>
<td>4.93 ± 2.04</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data is represented in the form of mean ± SD. p ≤ 0.05 is taken as statistically significant. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure; MDA, malondialdehyde; NO, nitric oxide.

Table-2: Correlation of all the study parameters with vascular age

<table>
<thead>
<tr>
<th>Vascular age (years)</th>
<th>Group-1 (n = 62)</th>
<th>Group-2 (n = 73)</th>
<th>Total study population (n = 135)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>r = 0.19 *</td>
<td>r = 0.38 *</td>
<td>r = 0.52 *</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>r = 0.24 *</td>
<td>r = 0.27 *</td>
<td>r = 0.45 *</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td>r = 0.04 *</td>
<td>r = 0.31 *</td>
<td>r = 0.37 *</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>r = 0.23 *</td>
<td>r = 0.34 *</td>
<td>r = 0.51 *</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MDA (μmol/L)</td>
<td>r = 0.16 *</td>
<td>r = 0.20 *</td>
<td>r = 0.46 *</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NO (μmol/L)</td>
<td>r = 0.03 *</td>
<td>r = -0.23</td>
<td>r = -0.41 *</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*p ≤ 0.05 is considered as statistically significant.

Table-3: Comparison of different age parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group-1 (n = 62)</th>
<th>Group-2 (n = 73)</th>
<th>Total study population (n = 135)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>40.27 ± 7.44</td>
<td>46.55 ± 6.43</td>
<td>43.67 ± 7.64</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Vascular age (years)</td>
<td>37.63 ± 10.75</td>
<td>55.07 ± 6.91</td>
<td>47.06 ± 12.65</td>
<td>&lt;0.00001</td>
</tr>
</tbody>
</table>
DISCUSSION

Our results help in developing the understanding that practicing yoga helps in decreasing oxidative stress and maintaining optimal endothelial function which in turn reduces the reactive oxygen species (ROS) and results in normalizing blood pressure. Our study also provides a direction toward the understanding that the advancement of ageing process occurs with an increase in blood pressure phenotypes regardless of practicing yoga for a short-term duration. One of the possible explainable reasons might be vascular age goes hand in hand with all the other parameters so it is quite obvious for the changes in the blood pressure phenotypes and the oxidative stress parameters. This finding of ours also might be due to our small sample size and bigger age group in the present study. We again consider this as one of our limitations in this study.

Previous studies done to solve the mystery of this intricate relationship between oxidative stress and vascular ageing have created a buzz in the scientific community which drove us to conduct our current study. We do corroborate the finding of our study with the study of Puca AA, et al. (2013) in this direction which enlightened the scientific community regarding the role of oxidative stress in the advancement of vascular ageing [6].

**Molecular mechanisms of oxidative stress induced vascular ageing:** Several mechanisms may be involved in the advancement of vascular age with oxidative stress such as endothelial dysfunction, inflammation, Vascular Smooth Muscle Cell Senescence (VSMCS) etc.

**Endothelial Dysfunction:** Endothelial cells play a pivotal role in maintaining vascular homeostasis by regulating vascular tone, inflammation, and thrombosis. Oxidative stress disrupts endothelial function by impairing nitric oxide (NO) bioavailability, promoting endothelial cell apoptosis, and increasing vascular permeability. Furthermore, ROS-mediated oxidative modification of lipids, proteins, and DNA within endothelial cells contributes development of a pro-inflammatory and pro-thrombotic vascular phenotype, predisposing to the development of age-related vascular diseases [7].
**Inflammation:** Chronic low-grade inflammation is a hallmark of the ageing process and is intimately linked to oxidative stress-induced vascular ageing. ROS activate redox-sensitive transcription factors such as nuclear factor kappa B (NF-kB), and activator protein-1 (AP-1), leading to the up-regulation of pro-inflammatory cytokines, adhesion molecules, and chemokines within the vascular wall. This perpetuates a vicious cycle of inflammation and oxidative stress, exacerbating vascular dysfunction and contributing to the pathogenesis of age-related vascular diseases [8].

**VSMCS:** Vascular smooth muscle cells (VSMCs) are key players in vascular remodeling and arterial stiffness, both of which are prominent features of vascular ageing. Oxidative stress induces premature senescence of VSMCs through various mechanisms, including telomere shortening, DNA damage, and mitochondrial dysfunction. Senescent VSMCs display altered secretory profiles characterized by the secretion of pro-inflammatory cytokines, matrix metalloproteinases (MMPs), and extracellular matrix (ECM) proteins, further perpetuating vascular dysfunction and contributing to the development of age-related vascular pathologies [9].

**Therapeutic strategies targeting oxidative stress in vascular ageing:** Understanding the molecular mechanisms underlying oxidative stress-induced vascular ageing has paved the way for the development of novel therapeutic strategies aimed at preserving vascular health in the ageing population such as antioxidant therapy, induction of anti-inflammatory agents, lifestyle interventions, and pharmacological modulation of senescence.

**Antioxidant therapy:** Administration of exogenous antioxidants, such as vitamin C, vitamin E, and N-acetylcysteine, may help mitigate oxidative stress and preserve endothelial function in ageing blood vessels [10].

**Anti-inflammatory agents:** Targeting inflammation using anti-inflammatory agents, such as nonsteroidal anti-inflammatory drugs (NSAIDs) or selective cytokine inhibitors, represents a promising approach for attenuating oxidative stress-induced vascular dysfunction [11].

**Lifestyle interventions:** Adoption of a healthy lifestyle characterized by regular physical activity, balanced nutrition, smoking cessation, and stress management can help reduce oxidative stress and promote vascular health in ageing individuals [12].
**Pharmacological modulation of senescence:** Pharmacological agents targeting senescent cells, such as senolytics or senomorphics, hold the potential for preventing or reversing vascular ageing by eliminating or modulating the harmful effects of senescent VSMCs [13].

Other explainable reasons for increased vascular age may include increased arterial stiffening due to an increase in blood pressure due to increased oxidative stress and endothelial dysfunction which in turn continue the vicious cycle of advancement in ageing [14, 15, 16].

**CONCLUSION**

Oxidative stress represents a common denominator underlying the pathophysiology of vascular ageing and age-related vascular diseases. By elucidating the molecular mechanisms linking oxidative stress to vascular dysfunction, novel therapeutic strategies targeting oxidative stress hold promise for preserving vascular health and reducing the burden of age-related cardiovascular diseases. Hence, we conclude our study by making it evident that yoga can help in delaying vascular age to an extent by decreasing oxidative stress. Further research efforts should focus on further unraveling the complex interplay between oxidative stress and vascular ageing to identify new therapeutic targets and improve clinical outcomes in the ageing population.
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