

# Biomechanical Prānāyāma Breathing Involves the Anti- Inflammatory Reflex of the Vagus Nerve in Survival Imputation

Giorgio Noera<sup>1\*</sup>, Matteo Ricci<sup>2</sup>, Enrico Ricci<sup>2</sup>, Boris Bazzani<sup>2</sup>, Marialuisa Vitobello<sup>1</sup>, Morena Gaddoni<sup>1</sup>, Donatella Barbagallo<sup>3</sup>, Raghuram Nagarathna<sup>4</sup> and Hongasandra Ramarao Nagendra<sup>4</sup>

<sup>1</sup>Giardino St Lucia Nursing Health Care and Telemedicine Unit, Italy

<sup>2</sup>Cardiology Clinic and Yoga Therapy Center, Italy

<sup>3</sup>Thabarwa Nature Centre EU, Italy

<sup>4</sup>S-VYASA University, Bengalûru, India

\*Corresponding author: Giorgio Noera, Health Ricerca and Sviluppo and Giardino St Lucia Telemedicine Unit Via St Lucia 30, 48024 Massa Lombarda (Ra), Italy

## ARTICLE INFO

**Received:** 📅 August 08, 2023

**Published:** 📅 November 14, 2023

**Citation:** Giorgio Noera, Matteo Ricci, Enrico Ricci, Boris Bazzani, Marialuisa Vitobello, Morena Gaddoni, Donatella Barbagallo, Raghuram Nagarathna and Hongasandra Ramarao Nagendra. Biomechanical Prānāyāma Breathing Involves the Anti- Inflammatory Reflex of the Vagus Nerve in Survival Imputation. Biomed J Sci & Tech Res 53(5)-2023. BJSTR. MS.ID.008451.

## ABSTRACT

The metabolism and homeostasis of living in thermodynamic laws is governed by both intrinsic and extrinsic innate and adaptive immunity in a temporospatial state. Neuronal reflexes that originate from tissue hypoxia and inflammasome are casual mass action kinetics for accelerated structural failure. Functionally the reflex is like Alfvén waves in structure-function interpolant of bio signal workflow. The physical layers that regulate response include the HPA axis, the Vagus Nerve, the reticuloendothelial and melanocortin systems. The metabolic function of Gibbs' free energy supply chain is to prevent imbalances as feedback errors in reflex arcs with Endotheliopathy induction. Vagus Nerve stimulation efficacy in anti-inflammatory treatment, is currently a framework for frequency emission devices regulatory approved in Europe and the United States for epilepsy, cardiac disorder and for acute respiratory distress. On the other hand, the ancient pattern of Prānāyāma has attributes in parasympathetic expression and objectification.

The neuro-arch effect, which involves stimulation of the Vagus Nerve by skeletal muscle and laryngeal frequency-emitting wavelets, suggests that every exercise leads to immune-mediated challenges. The 'Yoga-medical Prānāyāma ' was created by S-VYASA University, in collaboration with Western culture, to provide homecare respiratory distress related treatment. In Italy, a small ancillary sample size was tested for three time a day cycles in survival endpoint of SARS-COV-2 outbreak during February to May 2020 pandemic period. The dataset belongs to a protocol-compliant subgroup (trial identifier NCT04413747) in the first to second stage of virus infection. The Bayesian borrowing was ranked by sensitivity analysis in accordance with ICH E9 (R1) and stochastic demographic geolocation. The Weibull-k factor in inference resulted in probability distribution of 2.5 ratio as < 15% respiratory distress chance. The relative risk of death in daily rate was reduced 19-fold by Prānāyāma with significance level point estimate of  $p = 0.02$  in two-side CI 97.5 %.

**Keywords:** Pranayama Breathing Techniques; Vagus Nerve; Cholinergic Anti-Inflammatory Pathways; Response Criticality in Survival; Covid-19 Outbreak

**Abbreviations:** ARDS: Acute Respiratory Distress Syndrome; cAMP: Cyclic Adenosine Monophosphate; COVID-19: Coronavirus Disease SARS-CoV-2; DALYs; Disability-Adjusted Life Years; EMA: European Medicines Agency; FDA: Food and Drug Administration; GPCRs: G- Proteins-Coupled Receptors; HPA: Hypothalamic-Pituitary-Adrenal Axis; ICH: The International Council for Harmonization; IUPHAR/BPS: International Union of Basic and Clinical Pharmacology and British Pharmacological Society; PICO: Population/Problem/Patient; Intervention/Issue; Comparison; Outcome; POMC: Pro-Opio MelanoCortin; pdf: Probability Density Function; RCT: Randomized Controlled Trial; RR: Relative Risk; QALYs: Quality-Adjusted Life Years; VN: Vagus Nerve; S-VYASA; Swami Vivekananda Yoga Anusandhana Samsthana

## Introduction

The human hypothalamic-pituitary-adrenal axis and melano-cortin system represent the ancestral neuro-immune architecture of adaptability in the environment [1]. The constant across phylogenetic lines is the subset of the immune system in a hierarchical working agent for inter-operative and interdependence of other subsets. The bio-signals are the major players and regulation variables for encoding like-Alfvén low-frequency waves in structure-function interpolant workflow [2]. Hierarchically, end-of-life is the failure of host adaptative capabilities in high level of thermodynamic cycle of energy supply chain [3]. Energy production, oxidative phosphorylation and glycolytic processes are the intimate responses of self-maintenance in a flight of functional- structural change. Weight-energy need fluid in and out of volume equation and scales of instability by stressors lead to extremely critical body conservation [4]. Microcirculation and endothelial subset are the multi-state gate space for thermodynamics of living and failure [5].

The high-level overview is the G-Protein Coupled receptors (i.e., GPCRs) family to control the local stability of binding energy and molecular docking cross the supply chain [6]. For instance, by Pharmacological Target Guide, developed by International Union of Basic and Clinical Pharmacology and British Pharmacological Society (i.e., IUPHAR/BPS) experts, identified the hardness of GPCRs in a the two-spin operator for driving the cAMP-dependent pathway [7]. Physiologically, real-time casual power are proportional gradients of hypoxic hyperinflammation reflex that generate energy distribution beds of mass fixative exchange and loop in the principal metabolic processes that occur. In recent years, it has been established that the extra-HPA immune control channels, are in a widespread distribution and chemotaxis with Vagus Nerve (i.e., VN) anisotropy through intermediaries onto cells-mitochondrial dynamics [8].

## The Neuro-Immune Reflex

Nearly two decades the field research of “brain to immune system communication”, has elucidated the networking role of the inflammatory reflex [9]. The workload might be represented within a wired and wireless infrastructure of which the function is to over-order the hieratical control of microcirculation and oxygen flow transport to tissue and cells [10,11]. An anti-inflammatory role of the VN is observed using either vagal afferent and afferent’s, targeting cholinergic anti-inflammatory pathway by melanocortin receptor lies and GPCRs [12]. In this context, the VN provides a hub & spoke topology of a wired network information for brain stem circuits and response interface for neuro-releasing factor. This is in a leukocyte traffic controller for the endothelial microvascular glycocalx gatekeeper [13]. The loops finalize the acetylcholine release in the reticule-endothelial system and signal transduction for inhibition of pro- inflammatory mediator’s pathways up to suppressor of cytokine signaling that negatively regulate the Janus Kinase/signal transducers and activator of transcription proteins.

The plausibility and consistency of scientific data, constitutes the basis of therapeutic use of VN stimulation by medical electric devices equipment with current pulsed at 25 Hz through the skin for 2 minutes. Devices are currently 510k FDA and EMA [14] approved for patients aged >12 years with drug-resistant epilepsy, cardiac shock by arrhythmia and recently Health Canada has granted the emergency use authorization for COVID-19 for treating COVID-19 cytokine storm and acute respiratory distress syndrome. The expert opinion regard, various clinical studies have been verified the safety and efficacy [15]. Conceptually, devices-less VN subthreshold stimulation may be reached by forced mechanical thorax exercise linked to Alfvén OM mantra low-frequency equation from as censored 44.1 Kz to 2-fold emission by laryngeal vibration [16,17].

## Prānāyāma

Complementary and alternative medicine is defined by the World Health Organization as the broad set of health-care practices that are not part of that country’s own tradition and are not integrated into the dominant health-care system. In this context Prānāyāma is generally defined as breath control with laryngeal harmonic sound. In view of the full quality attributes for neuro-immune axis properties, there are efficacy evidence on Quality-Adjusted Life years (QALYs) and Disability-Adjusted Life years (DALYs) [18]. Apply PICO model for evidence-based medicine - i.e., Population/Problem/Patient; Intervention/ Issue; Comparison; Outcome - by University of Illinois Chicago for overall Yoga therapeutic intervention, systematically it is assessed safety [19]. The assessment of DALYs by the Consort statement’s meta-analyze, was statistically relevant in benefit for screened 92 RCT of 490 in eligibility for a total of 8,430 sample size statistical [20]. To our knowledge, Prānāyāma’s short-term assessment in life-threatening and emergency situations has not been censored as in Kaplan Maier survival Imputation (KMI).

## The Clinical Trial identifier NCT04413747

The above assumption, rationale of Prānāyāma and pattern in real-world occurrence, have been blamed on Covid-19, which has multiple tricks up its lethality and challenges faced by the - “Yoga Pranayama Adjuvant to Treat Burden COVID-19” [21]. The play on a web-based platform was intended to promote horizontal subsidiarity and research opportunities while temporarily self-organizing for public health measures. The data set for 100 cases of coronavirus disease between February and March 2020 was collected during the protocol evaluation and used for sensitivity analysis. The purpose of this subgroup is to decrease bias in non-randomized trials and data gaps in the context of enrolling after the protocol date. Rapid changes in health outcomes after May 2020, while taking into consideration the complexity of emergency response notifications. Bayesian borrowing was employed to present the before-and-after study in a homogeneous data [22].

## Material and Methods

Sensitivity analysis of Prānāyāma adjuvant in homecare by ICH E9 (R1) principle, was carried out on dataset of 100 enrolled consecutive confirmed SARS-CoV-2 infection [23]. The period was from February to May 2020, in the district of Emilia Romagna, in the north of Italy [24,25]. Paracetamol therapy for hyperpiesia without early anti-inflammatory drugs such as ibuprofen, corticosteroid up to hydroxychloroquine administration was the cut-off for inclusion criteria for homecare in the first-second stage of disease. The end point was 15-day mortality in hospitalization rate. The reviewer's design was in nonrandomized multi-state model and accelerated life-expectancy failure for early warning score NEWS2-COVID-19 alongside the full clinical assessment in primary care. Patients training and adjuvant treatment was for weekly repetitive cycles of "OM" laryngeal vibration and expiratory exercises onto Bhramari, Surya Bheda and Nadi Shodhana Prānāyāma in compressible language of Western culture and emergency studied by S-VYASA University Bengaluru, India.

DALYs and QALYs homecare was supervised by an ad hoc context for trained physicians, nurse, and physiotherapists in face-to-face consultation within a remote web-platform surveillance and intensive daily-line monitoring and testing. The offset test for efficacy in observed-to-expected outcome, was assessed in probability density function (pdf.) in a rank-preserving accelerated failure of life from per period daily epidemiological data. The time-to event in Kaplan Maier imputation (KMI) as Andersen-Gill recurrent event-time, were extracted by Official M-source statistic and used in Bayesian borrowing by the weight of pdf [26]. The reliability and efficacy were onto conditional Weibull survival in  $\beta$  shape and  $\eta$  characteristic of life where 62.3 % population have life-failure. Observe-to-Expected ratio as chi-squared test statistic for Prānāyāma contingently operator was compared with a posteriori-to-prior pdf. in  $k$  of  $\beta$  weight [25]. Parameters distribution were by conditional Weibull probability function  $F$ :  $(\text{future\_age} \mid \text{current\_age}) = 1 - e^{-[(\text{current\_age} / \eta)^\beta - (\text{future\_age} / \eta)^\beta]}$  [27]. The Relative Risk ratio (RR) and proportions defective of two side binomial confidence interval, were tested in point estimate of significance level.

## Results and Discussion

The 100 enrolled case were within age range of 50–69 year old as consecutive confirmed SARS-CoV-2 in principal stratum. The referred epidemiological data per area was of 666,299 with pooled age of 44 yr. among 4,458,000 inhabitant. The stochastic demography was male-female ratio of 48/52%, georeferencing north in Italy 174.5 inhabitant Km<sup>2</sup> density, mean age 46.6 yr., pooled expected life span of 82.4 yr. The general mortality rate of 13.3 x 1,000 in 2020 with increasing mortality rate per period of 17% with average of overall mortality from February to May of 22.553 cases of which 59.665, male 28.549 and female 31.116 [27]. In March 2020, 7,776 death more respect 2019 during first epidemic peak impact.

The estimate of lethality rate for COVID-19 per period was respectively for age range of 50-59 yr. and 60-69 yr. of 1.3 and 3.7 % with a pooled approximation "de minimis" with of coeval treatment of a pooled 2% for > 62 % in 15-day hospital death rate. The theater scenario was over 28 x 100,000 inhabitant, emergency calls per 100 hospital bed of which 2.2% for area medica and 1.8% intensive care unit. The probability density function truncated at 15-day mortality rate in infected- COVID-19 per area and age, give a probability life-failure of 0.02 in distribution and approximation for survival of  $k$  factor 6.5 in  $\beta$  shape and 14.92-day characteristic of life as 62 percentile parameters: pdf,  $f(t), R(7.00) = 1$ , mean life 14.27-day in  $\eta$  of 15-day distribution of characteristic life at right, unreliability  $F(t)$  0.434, Hazard rate  $f(t)/R(t)$  of 0.373 within the end of second week [27]. The Prānāyāma contingently operator with proper left Tobit's variable probability density risk assessment, resulted in observed no-event of 30-day mortality rate as life failure of 0.00,  $\beta$  shape block box of  $k$  factor > 15.

The coefficient in Weibull- $k$  factor resulted in breadth narrowed density of 2.5  $k$  ratio as > 15% more probability of living in "Hypergeometric Optimization of Motif Enrichment algorithm" as difference in Rayleigh non-negative variable equivalent to a Chi-square cumulative distribution [28]. The two side P-value proportions defective of binomial confidence interval of cases having event-free 15-day mortality rate, resulted 95% CI 42.07-to-55.93 and significant level of  $p < 0.0001$ . The Relative Risk (RR) two-side binomial CI 97.5 % was Lower bound 1.7 to Upper bound 2.306 was 1.98 as 19-fold decrease the risk of 15-day mortality rate. The for borrowing, resulted in point estimate a significance level of  $p = 0.02$  between lower  $p < 0.001$  and upper limit of  $p = 0.081$  values [29]. The Altman's Number Needed to Treat (NNT) was benefit 50.500 CI 74.63 (harmed)-to  $\infty$ - 18.85 (benefit) as the estimated number of patients who need to be treated with the new treatment rather than the standard treatment (or no treatment) for one additional patient to benefit. The Bayesian borrowing for a larger true effect size for COVID-19 lethality 2020 have made possible to adjust the type I error below 5% of  $\alpha$  inflation and increasing effect sizes.

## Conclusion

Inferential estimates with reliability enabled the efficacy of the Prānāyāma exercise as a Bayesian contingent operator in survival imputation for epidemiological exceptional conditions of the COVID-19 outbreak. Although many limitations exist, it is correct to cite Prānāyāma as adjuvants for mild to moderate cases of hyperinflammation. As of mid-March, there was no evidence to claim anti-inflammatory drugs to worsen infection, so some public health bodies only recommend taking acetaminophen. The daily mortality ratio from

COVID-19 was the primary estimate for care. The nested care for hyperinflammation may be considered a lowered confounding factor in this period. The primary data set's reliability analysis is credible under the circumstances because the survey is not randomized due to

the adjusted mortality rate harmonization. This implies that Prānāyāma can be considered safe and first-line in homecare containment of hyperinflammation disorders with a 19- fold decrease the risk in accelerated life-span failure.

## Acknowledgements

Major thanks”: to entire staff of Yoga Committees Ayush University Swami Vivekananda Yoga Anusandhana Samsthana, Antonio Gaddi MD PhD President of Italian Telemedicine Association Rome, Italy, Daniele Bassi Mayor of the Municipality of Massa Lombarda, Italy, Cheti Sereafini Head of Nurse Health Care Giardino St Lucia Massa Lombarda Italy.

## Conflict of Interest

We declare there are no financial interest, or any conflict of interest exists.

## References

- DeMorrow S (2018) Role of the Hypothalamic–Pituitary–Adrenal Axis in Health and Disease. *International Journal of Molecular Sciences* 19(4): 986.
- Alfvén H (1942) Existence of Electromagnetic- Hydrodynamic Waves. *Nature* 150: 405-406.
- Cleri F (2016) Thermodynamics for Living Systems. In: *The Physics of Living Systems. Undergraduate Lecture Notes in Physics*. Springer, Cham.
- Dutta A, Chattopadhyay H (2021) A Brief on Biological Thermodynamics for Human Physiology. *J Biomech Eng* 143(7): 070802.
- Broz P, Dixit V (2016) Inflammasomes: mechanism of assembly, regulation and signaling. *Nat Rev Immunol* 16(7): 407-420.
- Davenport AP, Scully CC, Chris de Graaf, Alastair JH Brown, Janet J Maguire (2020) Advances in therapeutic peptides targeting G protein-coupled receptors. *Nat Rev Drug Discov* 19(6): 389-413.
- Pawson AJ, Sharman JL, Benson HE, Elena Faccenda, Stephen P H Alexander, et al. (2014) The IUPHAR/BPS Guide to PHARMACOLOGY: an expert-driven knowledgebase of drug targets and their ligands. *Nucleic Acids Res* 42(Database issue): D1098-D1106.
- Olofsson P (2018) Vagus Nerve Stimulation and Regulation of Inflammation. In: Elliot S. Krames, P Hunter Peckham, Ali R Rezai (Eds.), *Neuro-modulation* (2<sup>nd</sup> Edn.), Academic Press, pp. 1483-1492.
- Schiller M, Ben-Shaanan TL, Rolls A (2021) Neuronal regulation of immunity: why, how and where? *Nat Rev Immunol* 21: 20–36.
- Munteanu C, Călin Dragoș MA, Popescu Mădălina MC, et al. (2023) Current data regarding homeostasis of tissues oxygenation in pathophysiological and therapeutic circumstances. *Balneo and PRM Research Journal* 14(2): 565.
- Giacomello M, Pyakurel A, Christina Glytsou, Luca Scorrano (2020) The cell biology of mitochondrial membrane dynamics. *Nat Rev Mol Cell Biol* 21: 204-224.
- Ge Yj, Liao Qw, Xu Yc, Qiang Zhao, Bei-li Wu, et al. (2020) Anti-inflammatory signaling through G protein-coupled receptors. *Acta Pharmacol Sin* 41: 1531-1538.
- Moore KH, Murphy HA, M George EM (2021) The glycocalyx: a central regulator of vascular function *American Journal of Physiology-Regulatory Integrative and Comparative Physiology* 320(4): R508-R518.
- Mertens A, Raedt R, Stefanie Gadeyne, Evelien Carrette, Paul Boon, et al (2018) Recent advances in devices for vagus nerve stimulation. *Expert Rev Med Devices* 15(8): 527-539.
- McIntire LK, McKinley RA, John P McIntire, Rebecca D Brown, et al. (2021) Cervical transcutaneous vagal nerve stimulation (ctVNS) improves human cognitive performance under sleep deprivation stress. *Commun Biol* 4(1): 634.
- Gurjar A, Ladhake SA, Thakare AP (2009) Analysis Of Acoustic of “OM” Chant To Study It’s Effect on Nervous System.
- XQ Lu, LM Yu, W Guo, KH Li (2021) Ion flow driven by low frequency Alfvén waves in a low-beta plasma. *Physics of Plasmas* 1 February 28(2): 022903.
- Cramer H, Ward L, Robert Saper, Daniel Fishbein, Gustav Dobos, et al. (2015) The Safety of Yoga: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *American Journal of Epidemiology* 182(4): 281-293.
- Kanchan J, Thapliyal A (2021) Physiology of Pranayama. *International Journal for Modern Trends in Science and Technology* 7(8): 116-119.
- Jayawardena R, Ranasinghe P, Himansa Ranawaka, Nishadi Gamage, Dilshani Dissanayake, et al (2020) Exploring the therapeutic benefits of Pranayama (yogic breathing): A systematic review. *Int J Yoga* 13(2): 99-110.
- Clinical Trial gov. identifier NCT04413747 Protocol.
- Marušić M F, Fidahić M, Cepeha C M, Loredana Gabriela Farcaș, Alexandra Tseke, et al. (2020) Methodological tools and sensitivity analysis for assessing quality or risk of bias used in systematic reviews published in the high-impact anesthesiology journals. *BMC Med Res Methodol* 20: 121.
- (2020) EMA/CHMP/ICH/436221/2017, ICH E9 (R1) addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials.
- (2021) IHME COVID-19 Forecasting Team, Modeling COVID-19 scenarios for the United States. *Nat Med* 27: 94-105.
- Official website of Emilia Romagna Region, Italy. Available at data from decessi-regionali\_1-23082023.xlsx - live.com.
- Kaplan D, Chen J, Yavuz S, Weicong Lyu (2023) Bayesian Dynamic Borrowing of Historical Information with Applications to the Analysis of Large-Scale Assessments. *Psychometrika* 88: 1-30.
- Nelson W (2003) *Applied Life Data Analysis*, Wiley-Interscience; (1<sup>st</sup> Edn.), edition Print.
- Heinz S, Benner C, Spann N, Eric Bertolino, Yin C Lin, et al. (2010) Simple Combinations of Lineage-Determining Transcription Factors Prime cis-Regulatory Elements Required for Macrophage and B Cell Identities. *Mol Cell* 38(4): 576-589.
- Neubauer J (2014) Battery Lifetime Analysis and Simulation Tool (BLAST) Documentation, NREL/TP-5400- 63246.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2023.53.008451

Giorgio Noera. Biomed J Sci & Tech Res



This work is licensed under Creative Commons Attribution 4.0 License

Submission Link: <https://biomedres.us/submit-manuscript.php>



#### Assets of Publishing with us

- Global archiving of articles
- Immediate, unrestricted online access
- Rigorous Peer Review Process
- Authors Retain Copyrights
- Unique DOI for all articles

<https://biomedres.us/>