Article

The effect of the human regenerator jet device on the quality of life of adult individuals

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Abstract

Quality of life (QoL) encompasses physical, mental, and social health; values; independence; social relationships; environmental interactions; work-life quality; and productivity. Chronic physical and psychological stressors affect QoL negatively and lead to the development of several disorders or diseases. This study aims to evaluate the effects of a device that generates and applies Cold Atmospheric Plasma (CAP+) to the entire human body, the Human Regenerator Jet Device (HR), on the Quality of Life of adult individuals in Greece [HR-QoL]. Here, we report the First-in-Human beneficial effects of HR in a crossover, single-blind clinical study of individuals with chronic stress, chronic pain and fatigue, sleep disorders, and long-COVID syndrome. Future

studies will focus on disease and regenerative processes to further evaluate the HR-CAP+ effect on human homeostasis and disease.

Keywords: Human Regenerator Jet, cold atmospheric plasma (CAP), medically unexplained symptoms (MUS), chronic pain and fatigue, sleep disorders, Long/Covid

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INTRODUCTION

Quality of life (QoL) is one of the most critical outcomes in health-care programs[1]. QoL is an individual, multidimensional, and latent concept encompassing objective and subjective factors that reflect an individual's physical, mental, and social health[2-4]. The World Health Organization (WHO) also defines QoL as: "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns[5]. This concept encompasses physical health, mental health, independence, social relationships, personal values, and interactions with the environment. As a result, it is unsurprising that QoL influences the work-life quality and, consequently, productivity at work[6-7].

All organisms must sustain homeostasis, which is continually challenged by internal or external stressors. Stress transpires when homeostasis is compromised; it is reestablished through physiological and behavioral responses mediated by the stress system within both the central nervous system and peripheral organs[8]. Stress has a detrimental effect on QoL, correlating with diminished job performance, elevated medical expenses[9-10], and compromised mental and physical health associated with psychological pressure[11-12]. Persistent environmental stressors can precipitate chronic conditions such as fibromyalgia, which is characterized by chronic pain, fatigue, sleep disturbances, and cognitive impairments. Treatment strategies aim to mitigate pain and enhance activity levels through personalized plans that encompass education, exercise, mental techniques, and pharmacological interventions; however, individual responses to these treatments vary[13]. Viral infection-related stressors can produce comparable long-term effects extending beyond the incubation period, exhibiting symptoms such as severe fatigue and "brain fog," collectively termed "Post-COVID/Long-COVID"[14-15]. Thus, it is increasingly apparent that innovative therapeutic approaches must be developed to address chronic stress, pain, fatigue, sleep disorders, and Long-COVID, thereby improving the quality of life for affected individuals worldwide.

Plasma medicine represents an emerging interdisciplinary domain that encompasses physicists, biologists, and medical practitioners[16-20]. Plasma is characterized as “a quasineutral gas containing free electrons and ionized atoms and molecules with collective behavior from long-range coulomb forces,” which generates electric and magnetic fields, as well as currents[21-23]. It is categorized into high-temperature, thermal, and non-thermal (cold) plasma types. High-temperature plasma consists of particles in a uniform thermal state, whereas non-thermal or cold plasma comprises particles not in thermal equilibrium. Cold plasma, produced at low or atmospheric pressure (CAP) has been rigorously evaluated for multiple purposes, such as wound treatment in both animals and humans; as an antimicrobial agent in dentistry; as a facilitator of the proliferation and differentiation of stem and progenitor cells (including adipose-derived, osteoprogenitors, mesenchymal, hematopoietic, and neural cells); for the regeneration of nasal mucosa, bronchial epithelial, and neural tissues in animal models; for the induction of anti-proliferative, pro-apoptotic, and immunogenic cell death in various cancer cell lines in culture, and for its potential in immunotherapy, demonstrating potent anti-tumor effects in mice with CAP-treated T cells[17-18,20]. Use of small CAP devices is primarily limited to aesthetic and dental procedures; however, their medical applications are currently under active investigation. Most research has focused on cell culture and animal models; thus, extensive studies involving human subjects on disease treatment and regenerative processes are needed to assess the benefit of CAP application to humans.

Here, we present the First-in-Human effects of a novel CAP+-whole body treatment electronic bed device, the Human Regenerator Power Jet, in the context of a crossover single-blind clinical study for individuals with chronic stress, chronic pain and/or fatigue, sleep disorders, and the Long-COVID Syndrome, conditions that affect the QoL among adults in Greece and worldwide [HR-QoL].

METHODS- STUDY DESIGN

Participants

Of 62 potential participants who were screened, 18 did not meet eligibility criteria and were excluded [Figure 1]. Before the study began, 4 participants withdrew. Eventually, the HR-QoL crossover, single-blind clinical study recruited 40 participants and randomized them into two groups (A & B). Group A (20 adults) was treated at the HR under CAP conditions (CAP Effect) (10 sessions), followed by a 1-month wash-out period, before treatment at the HR under AIR Conditions (Sham Device-Placebo Effect). Group B (20 adults) was treated at the HR under AIR conditions (Sham Device-Placebo Effect) followed by a 1-month wash-out period, before treatment at the HR under CAP Conditions (Cap Effect). The participants were unaware whether they were exposed to CAP or AIR from the device. In the HR-QoL study, "adults" are defined as individuals aged 18 years or older. Eligible participants of both sexes were aged 18 to 94 years. The inclusion criteria included male and female participants with a diagnosis of chronic stress, chronic pain, and/or chronic fatigue, and Post/Long-COVID Syndrome. The exclusion criteria included: a) pregnancy or Breastfeeding period, b) participation in another stress-related study, c) presence of implanted devices, d) major psychiatric disorder, and e) extreme mobility issues. The eligible list of participants was evaluated by the Clinical and Translational Research Endocrine Unit of the National and Kapodistrian University of Athens (NKUA).

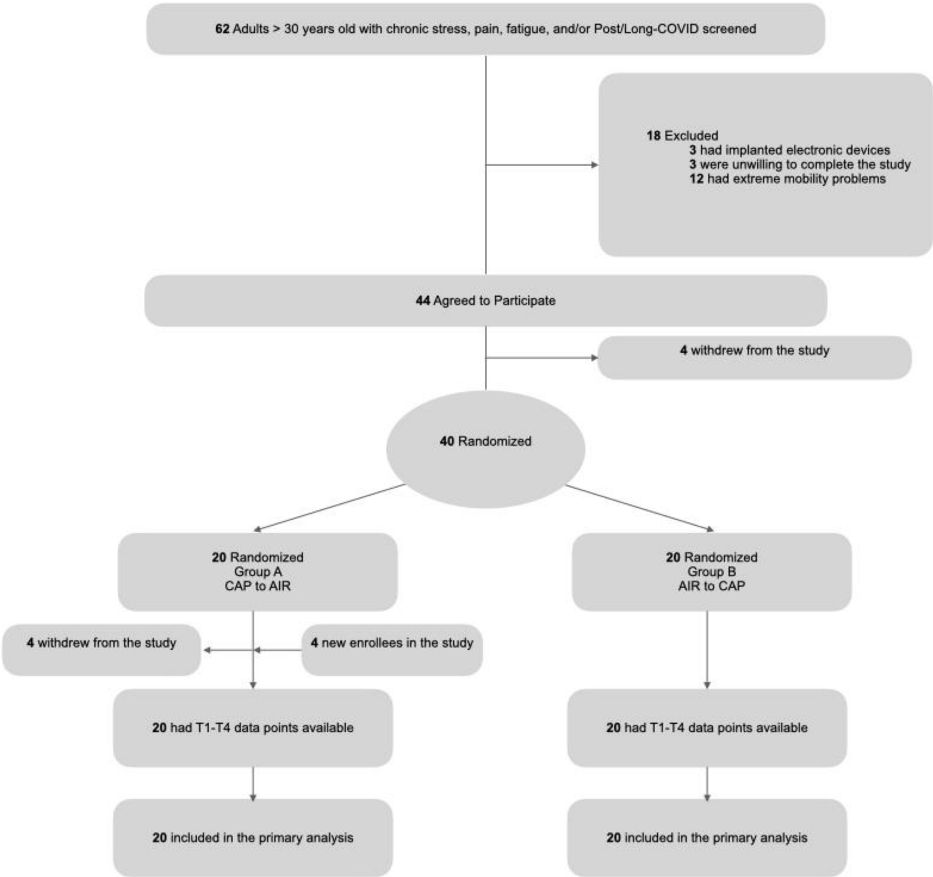


Figure 1. Flow chart depicting participant selection.

Clinical protocol

The HR-QoL is a crossover, single-blind study on the effects of the Human Regenerator Devices on the Quality of life of adult individuals in Greece. The participants had: a) hematological, biochemical, and endocrinological tests, including biomarker analysis (cortisol, hsCRP). 20 mL of blood were taken from the participants to examine the he physiological function of the hematopoietic system (hematocrit, hemoglobin, hemoglobin concentration, white blood count, platelet count), the kidneys (urea, creatinine), the liver (SGOT, SGPT, γ-GT), the thyroid gland (TSH, fT3 and fT4) and electrolyte homeostasis (sodium, calcium, magnesium, potassium, bicarbonates) and C-reactive protein (hsCRP) to assess inflammation. Sampling was done at four time points: T1: baseline, Initiation date; T2: at 3 weeks, completion of the first cycle of CAP/AIR treatment (10 sessions every other day); T3: at 7 weeks, initiation of the first cycle of AIR/CAP treatment (10 sessions every other day); T4: at 10- 11 weeks, completion date. In addition, salivary cortisol was measured four times per day at T1, T2, T3, and T4. The initial day sample was measured during awakening, the second 20 mins later, the third at 20:00, and the last at 23:00. Each participant was trained to insert the end of a cotton swab into their mouth for 2 min, or to chew the edge of a cotton swab for 1-2 min. Then, the swab was placed inside a plastic transport tube and kept in the refrigerator at 0-4 °C. The samples are returned to the clinic for further processing.

b) Bioimpedance measurements were conducted with a BIA-ACC device (Biotekna srl, Venice, Italy). This full-body bioimpedance device is used for body composition analysis (Bioelectrical Impedance Analysis)[24]. Heart Rate Variability (HRV) was measured using the PPG-Stress Flow Device via photoplethysmography. HRV is a biomarker of autonomic nervous system function and is particularly important in participants with inflammatory diseases, given the anti-inflammatory action of the parasympathetic system[25].

c) All participants responded to the official Euro-QoL EQ-5D-5L and the Medically Unexplained Symptoms (MUS) questionnaires, and a brief pain & multidimensional fatigue inventory, perceived stress & state-trait anxiety inventory questionnaires at the T1, T2, T3, and T4 time points. The Greek versions of the Qualified Questionnaires were used to assess pain, sleep, fatigue, stress, anxiety, and QoL-demographic data, medical history, Daily routine, QoL, and treatments were evaluated (EQ-5D-5L)[26-27].

EURO-QOL: Quality of life health assessment questionnaire (License 62101)(in Greek):

The 5-level EQ-5D version (EQ-5D-5L) was introduced by the EuroQoL Group in, and it essentially consists of 2 pages: the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS). The descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has five levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The individual is asked to indicate their health status by ticking the box next to the most appropriate statement for each of the five dimensions (1-digit number/dimension). The five dimensions can be combined into a 5-digit number that describes the participant's health state, and reflects the overall health status of each individual (0-1 scale). The EQ VAS records the self-rated health of each participant on a vertical visual analogue scale, where the endpoints are labelled 'The best health you can imagine' and 'The worst health you can imagine' (0-100 scale). For the analysis, the United States Valuation of EQ-5D-5L Health States, using an international protocol, was applied[28].

Human regenerator jet device

The Human Regenerator Jet is a unique high-tech electronic bed device for Physical Wellness (System4 Technologies GmbH, CE2022) that generates and applies CAP throughout the human body [Figure 3][20]. It uses ambient air ionized by an over-30,000-volt energy source. The Human Regenerator Power Jet is a novel direct CAP device in which a high-voltage source serves as the active electrode and a grounded human body as the counter electrode (CAP+). Unlike traditional direct dielectric barrier discharge (DBD) devices, this system lacks a fixed dielectric counter electrode. No conventional dielectric barrier is present; instead, the user is an integral part of the electrical circuit. Ambient air at atmospheric pressure circulates between the two electrodes and serves as the working gas. By applying a high-frequency or pulsed high voltage, a strong electric field is generated in the air gap. Once this field exceeds the air's breakdown strength, free electrons are accelerated and collide with neutral air molecules (N_2, O_2, H_2O). This leads to impact ionization, excitation, and dissociation, thereby forming an ionized plasma. This approach is often referred to as direct plasma or floating-electrode dielectric barrier discharge. The plasma remains cold because energy is primarily transferred to the electrons, whereas the heavier particles (ions and neutrals) retain ambient temperature. The thermal stress on the tissue is therefore low. Due to its electrical impedance, capacitance, and grounding, the human body acts as a current-limiting counter electrode. This typically produces a corona discharge with limited current, enabling its application to living tissue.

Notably, CAP+ generation and effectiveness depend strongly on body geometry, jet-to-skin distance, skin condition, and electrical properties, thereby making it a truly personalized treatment. The dimensions of the device are 250 × 235 × 130 cm (Length × Width × Height), weighs 280kg, operates at 220-230V (50/60Hz), and has a power consumption of min. 10W to max. 120W. During the session, 20 mini-generators (mini-JETS) produce CAP, which activates cells via anions, electrons, and static energy. The Human Regenerator Jet enables application of CAP throughout the body to promote cell regeneration, cell charging, and neutralization of free radicals.

The model used in this study is the Human Regenerator Power Jet. The successful operation of the device is affected by environmental conditions at the installation site, with optimal conditions of use being for humidity around 50% and a room temperature of 16-24 °C. The Human Regenerator Jet is operated by qualified, trained staff (Operators) whose names are listed in the application book. Before they were allowed to use the device, operators completed a 1-day training course with System4 Technologies GmbH, after which they received an official certificate. The device has four applicators with electrodes, two for the arms and two for the legs, which come in contact with dry skin and enhance the CAP effect on the entire body. The device operator applies the applicators to the user and removes them after a 30-min CAP application. Once the user lies in a comfortable position on the device, the operator can press the start button on the control pad to initiate a session.

During the session, the user experiences a light tingling sensation and, in most cases, a light hiss. Most users report feeling relaxed and/or energized, and some may fall asleep. A slight ozone odor is also noticeable, resulting from the ionization effect. After the session, intake of at least 0.5 L of water is strongly recommended. System4 Technologies GmbH monitors all installed devices worldwide and has not received reports of side effects or intolerance to CAP+ to date. Since the Human Regenerator JET works by just gently energizing the human body, it is contraindicated for use in patients wearing implantable electronic health devices (pacemakers, cardiac resynchronization therapy (CRT) devices, insulin/pain pumps, implantable cardioverter-defibrillators (ICDs), left ventricular assist devices (LVADs), and others). Damage to these electronic devices can pose a potential risk to the user's life. For safety reasons, the use of the Human Regenerator Jet is not recommended for pregnant women, children younger than 10 years old, and users with a burdensome history of heart disease and stroke. Users with wet skin, those who weigh more than 180kg, those who suffer from epileptic seizures, those who are seriously ill, unconscious, anesthetized, confused, and unable to communicate are not permitted on the device. Treatment with CAP+ was performed at the Corpus Regen Wellness Center (Athens), using the Human Regenerator Power Jet as our model device, which was available to the participants for the duration of the study.

Statistical analysis

Data were described using median and range in all cases to account for the relatively small number of measurements. However, means and standard deviations were also calculated to assess skewness in the data. Nonparametric tests for repeated measures and one between-factor were applied using the F1-LD-F1 Design in the nparLD function in R. The analysis yielded statistical significance estimates for the within- and between-factor terms and their interactions, and pairwise comparisons were subsequently conducted using the Holm-Bonferroni criterion to adjust for multiple comparisons and control for α-level inflation. All statistically significant results are reported after adjusting for the α level. RStudio v. 2024.12.1 (2025-02-02) for Windows was used to conduct all statistical analyses.

RESULTS

The HR-QoL single-blind crossover study evaluated the effects of a novel cold atmospheric plasma (CAP+) jet producing device, the Human Regenerator Power Jet device [Figure 3], for individuals who suffer from chronic stress, chronic pain, chronic fatigue syndrome, sleep disorders, and Long-COVID Syndrome, all conditions that affect the QoL among adults in Greece [Figure 1, Table 1]. The HR-QoL study has solicited 40 participants randomized into two groups (A & B) in a 1:1 ratio. Group A (20 adults) was treated at the Human Regenerator Power Jet device under CAP conditions (CAP Effect) (10 sessions), followed by a 1-month wash-out period, before treatment at the HR under AIR Conditions (Sham Device-Placebo Effect) (10 sessions). Group B (20 adults) was treated at the HR under AIR conditions (Sham Device-Placebo Effect) (10 sessions), followed by a 1-month wash-out period, before treatment at the HR under CAP Conditions (Cap Effect) (10 sessions) [Figure 2]. The participants were unaware whether they were exposed to CAP or AIR from the device. The data collections time points were T1: baseline, Initiation date; T2: at 3 weeks, completion of the first cycle of CAP/AIR treatment (10 sessions every other day); T: at 7 weeks, initiation of the first cycle of AIR/CAP treatment (10 sessions every other day); T4: at 10- 11 weeks, completion date [Figure 1]. The protocol is described in detail in Figure 2. Demographic analysis of the participants showed that the male-to-female ratio for Group A was 30:70 (%) and for Group B 40:60 (%). Group A: Group B age ratios ranging from 30-39 at 5:5 (%), 40-49 at 15:20 (%), 50:59 at 25:20 (%), 60-69 at 40:35 (%), 70-79 at 10:15 (%), 80-89 at 0:5 (%), and ≥ 90 years at 5:0 (%). The mean age for Group A was 59,55 years, and for Group B, 59,65 years. Group A: Group B ratios (%)

for education level showed that elementary school graduates were 0:5 (%), high school graduates 10:0 (%), lyceum graduates 40:30 (%), university graduates 40:35 (%), MSc/MBA graduates 10:15 (%), and PhD graduates 0:15 (%). The participants suffered from chronic stress (100%) in both Groups A & B. Chronic pain stemming from several chronic diseases, such as osteo- and rheumatoid arthritis, joint and back pain, fibromyalgia stemming from cerebral palsy and arthritis, from medically unexplained symptoms (MUS), and included participants suffering from severe headaches and migraine [Table 1]. The majority of the participants in Group B (70%) and almost half in Group A (45%) (57,5 % in total) suffered from insomnia and 40% in Group A and 65% in Group B suffered from severe fatigue and Brain Fog, symptoms that appeared prominent in the Post-COVID/Long-COVID participants (10% in Group A and 30% in Group B), only to include in addition to those elevated anxiety and depression as well [Table 1].

Table 1. List of Participants in the HR-QoL Study.

Condition	Definition	Participant Condition or Disease	Group A (%)	Group B (%)
Chronic Stress	Chronic stress is the physiological or psychological response induced by a long-term internal or external stressor, either physically present or recollected.	-Anxiety -Depression	20 (100)	20 (100)

Chronic Pain	Chronic pain is pain that persists or recurs for longer than three months, and often becomes the sole or predominant clinical problem.	- Arthritis (osteoarthritis, rheumatoid arthritis) - Joint Pain (knee, shoulder) - Back pain (lower back pain) - Fibromyalgia (cerebral palsy, rheumatoid arthritis, Medically Unexplained Symptoms (MUS)) - Headache and migraine	17 (85)	18 (90)
Sleep Disorders	Sleep disorders include insomnia, obstructive sleep apnea, parasomnias, narcolepsy, and restless leg syndrome, which are difficulties linked to both physical and emotional problems.	- Insomnia	9 (45)	14 (70)
Chronic Fatigue	Chronic Fatigue Syndrome is a debilitating condition characterized by severe fatigue, cognitive dysfunction, sleep problems, autonomic dysfunction, and post-exertional malaise	-Severe Fatigue -Brain Fog -Insomnia	8 (40)	13 (65)

Post-COVID Long-COVID	Post/Long-COVID syndrome is characterised by persistent ongoing symptoms not explainable by an alternative diagnosis, three months after SARS-CoV-2 infection, including fatigue, brain fog, headache, sleep problems, dizziness, chest pain, depression, anxiety, joint or muscle pain.	-Severe Fatigue -Brain Fog -Anxiety -Depression -Chronic pain	2 (10)	6 (30)

Table 2. Arms & Interventions.

Arms	Intervention / Treatment
Active Comparator : CAP to AIR	Device: Cold Atmospheric Plasma (CAP)
Group A (20 adults) was subjected to Cold Atmospheric Plasma (10 sessions) generated by the Human Regenerator Power Jet device (Active Device: CAP Effect), followed by a 1-month wash-out period, before being subjected to AIR (10 sessions) (Sham Device-Placebo Effect).	The Human Regenerator Jet Device CAP Effect interventions include a 30-minute CAP exposure for participants every other day, for a total of 10 sessions (T1-T2).
	Device: Atmospheric Air (AIR)
	The Human Regenerator Jet Device AIR Effect interventions include a 30-minute exposure of subjects to Atmospheric Air every other day, for a total of 10 sessions (T3-T4).
Sham Comparator: AIR to CAP	Device: Atmospheric Air (AIR)

Group B (20 adults) was subjected to AIR (10 sessions) generated by the Human Regenerator Jet device (Sham Device-Placebo Effect), followed by a 1-month wash-out period, before being subjected to Cold Atmospheric Plasma conditions (10 sessions) (Active Device-CAP Effect).	The Human Regenerator Jet Device AIR Effect interventions include a 30-minute exposure of subjects to Atmospheric Air every other day, for a total of 10 sessions (T1-T2). Device: Cold Atmospheric Plasma (CAP) The Human Regenerator Jet Device CAP Effect interventions include a 30-minute CAP exposure for participants every other day, for a total of 10 sessions (T3-T4).

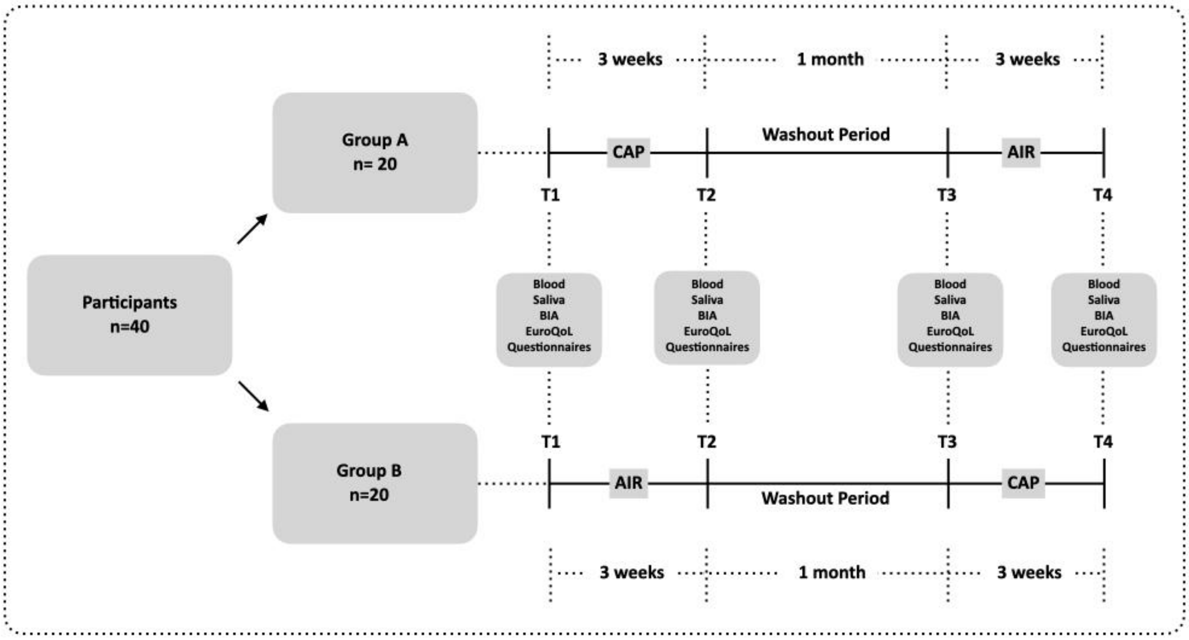


Figure 2. Clinical Study Protocol.

The EQ-5D-5L is a standardized health status measure developed by the EuroQol Group (EuroQol Group, 1990). It provides a simple instrument for describing and valuing health status across a wide range of disease areas. The participants completed the Greek version of a short descriptive system questionnaire and a visual analogue scale (EQ VAS), which took a few mins to complete. The distribution responses for

Groups A & B over time are presented in Table 3. In light green, the T1 and T4 time points are highlighted to show that both Groups at the end of the study experienced the beneficial effects of CAP [Table 3] across all dimensions [Table 3 and Figure 4] at the end of the study. The self-care dimension already had high baseline values, as this was a requirement for participant inclusion in the study [Table 3]. Based on EQ-5D-5L scores for the Values for Health State, the CAP application improves the overall health of participants in Groups A and B [Figures 5A & 5 B and Table 3]. Most participants in Group A, who were treated with CAP first, experienced beneficial effects during the washout period and continued to improve until the end of the study [Table 3, T1 to T4, and Figure 6A]. The placebo effect (AIR) primarily affected stress levels, reducing stress, anxiety/depression equally in the AIR condition of Group B (T1-T2) and in the CAP condition of Group A (T1-T2).

CAP was instrumental in reducing pain/discomfort and, consequently, inflammation, as symptom amelioration, which was observed only with CAP in both Groups A (T1-T2) & B (T3-T4) [Table 3; Figure 4; Figure 5A, B &C]. Amelioration of pain and fatigue symptoms leads to improved everyday activities and mobility, restores energy levels [Table 3; Figure 4; Figure 5A, B &C], and is followed by improved sleep patterns. Fewer than 5% of participants who did not experience symptom improvement reported at the end of the study that they did not feel comfortable lying on the bed, especially when CAP was applied, presumably due to changing positions on the bed, which alters the distance of the body from the mini jets and, in turn, lowers CAP efficacy. The above observations strongly suggest that the bed design contributes to human comfort and relaxation, thereby facilitating efficient CAP absorption when the body is positioned correctly [Figures 3, 4, 5].

Table 3. Distribution of EQ-5D-5L dimension responses for Groups A and B over time.

Dimension	Participants (%) T1		Participants (%) T2		Participants (%) T3		Participants (%) T4	
	A	B	A	B	A	B	A	B
MOBILITY								
No problems	6 (30%)	10 (50%)	8 (40%)	10 (50%)	7 (35%)	10 (50%)	9 (45%)	13 (65%)
Slight problems	5 (25%)	3 (15%)	7 (35%)	6 (30%)	7 (35%)	6(30%)	6 (30%)	5 (25%)
Moderate problems	5 (25%)	5 (25%)	2 (10%)	2 (10%)	3 (15%)	2 (10%)	4 (20%)	2 (10%)
Severe problems	4 (20%)	2 (10%)	3 (15%)	2 (10%)	3 (15%)	2 (10%)	1 (5%)	0 (0%)
Extreme problems	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SELF-CARE								
No problems	17 (85%)	15 (75%)	18 (90%)	19 (95%)	16 (80%)	19 (95%)	16 (80%)	18 (90%)
Slight problems	3 (15%)	5 (25%)	2 (10%)	1 (5%)	2 (10%)	1 (5%)	2 (10%)	2 (10%)
Moderate problems	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (10%)	0 (0%)	2 (10%)	0 (0%)
Severe problems	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Extreme problems	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
USUAL ACTIVITIES								
No problems	7 (35%)	9 (45%)	12 (60%)	15 (75%)	10 (50%)	13 (65%)	12 (60%)	14 (70%)
Slight problems	4 (20%)	6 (30%)	6 (30%)	2 (10%)	6 (30%)	5(25%)	4 (20%)	4 (20%)
Moderate problems	7 (35%)	4 (20%)	2 (10%)	2 (10%)	3 (15%)	1 (5%)	1 (5%)	1 (5%)
Severe problems	2 (10%)	0 (0%)	0 (0%)	1 (5%)	1 (5%)	1 (5%)	3 (15%)	1 (5%)
Extreme problems	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
PAIN/DISCOMFORT								
No problems	4 (20%)	3 (15%)	6 (30%)	3 (15%)	4 (20%)	2 (10%)	7 (35%)	8 (40%)
Slight problems	2 (10%)	8 (40%)	6 (30%)	8 (40%)	9 (45%)	10 (50%)	5 (25%)	6(30%)
Moderate problems	9 (45%)	6 (30%)	7 (35%)	6 (30%)	4 (20%)	5 (25%)	5 (25%)	4 (20%)
Severe problems	5 (25%)	2 (10%)	1 (5%)	2 (10%)	3 (15%)	3 (15%)	3 (15%)	2 (10%)
Extreme problems	0 (0%)	1 (5%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ANXIETY/DEPRESSION								

No problems	2 (10%)	1 (5%)	5 (25%)	3 (15%)	4 (20%)	3 (15%)	10 (50%)	8 (40%)
Slight problems	6 (30%)	5 (25%)	11 (55%)	5 (25%)	9 (45%)	4 (20%)	5 (25%)	1 (5%)
Moderate problems	7 (35%)	8 (40%)	3 (15%)	11 (55%)	6 (30%)	10 (50%)	5 (25%)	8 (40%)
Severe problems	4 (20%)	5 (25%)	1 (5%)	1 (5%)	1 (5 %)	3 (15%)	0 (0%)	3 (15%)
Extreme problems	1 (5%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Figure 3. The Human Regenerator Power Jet Device. (with permission from System4 Technologies GmbH, Germany).

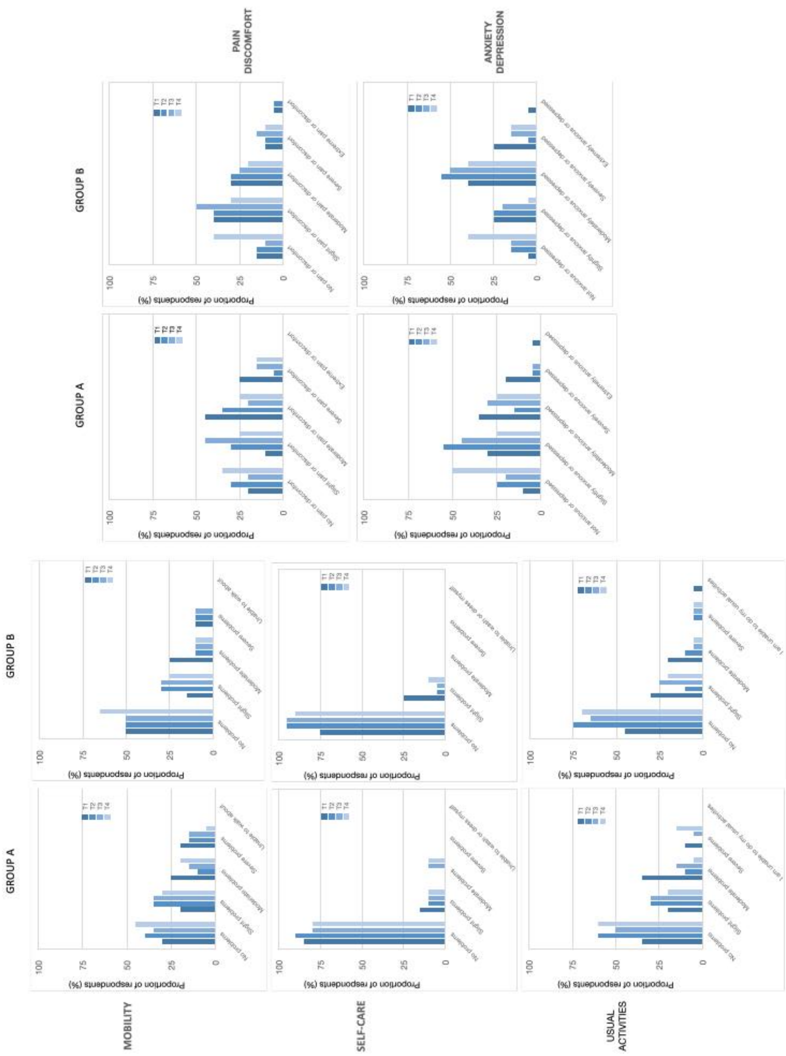
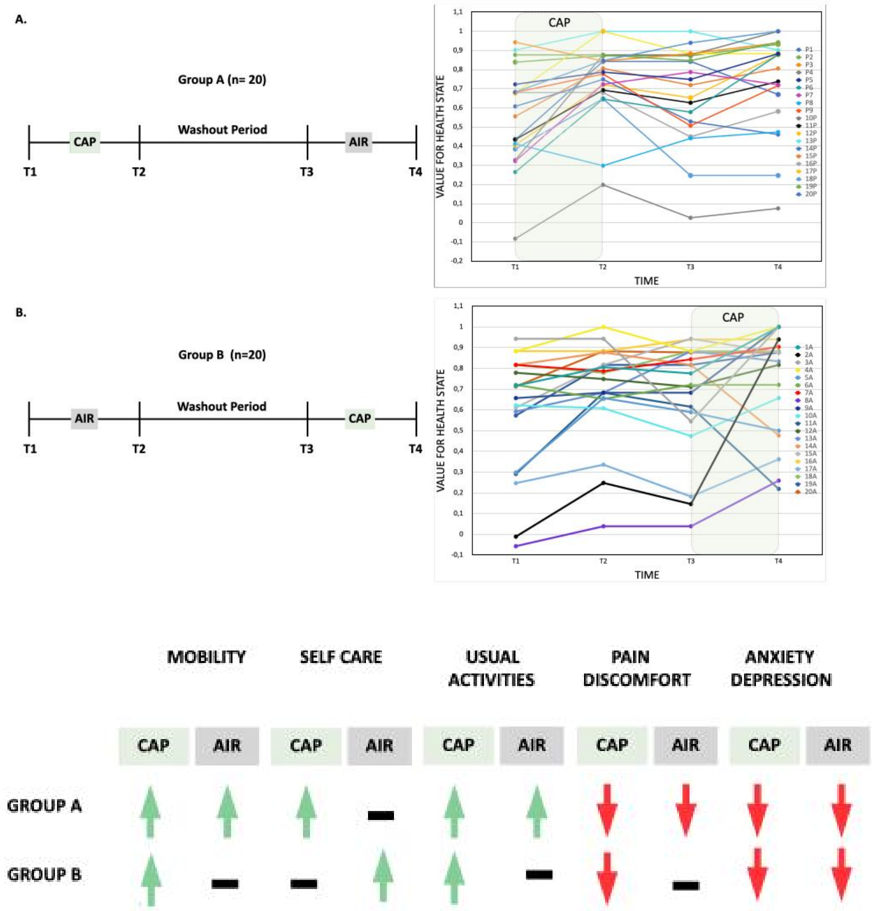


Figure 4. Proportion of responses for Mobility, Self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression by level of severity for EQ-5D-5L dimensions over time (T1-T4) for Group A and Group B participants.



C.

Figure 5. CAP+ treatment with the Human Regenerator Power Jet device improves participants' quality of life. Graphs depict changes in Values for the Health State over the duration of the HR-QoL study for (A) Group A and (B) Group B participants. CAP+ treatment periods are highlighted in light green. C. Graphical representation of the HR-QoL study results. EUROQoL: Red arrow, reduction; Green arrow, increase; black line, no change.

Blood analyses over time for Group A and Group B, covering hematological, biochemical, and endocrinological factors, revealed several notable differences [Figure 6]. The study on monocytes (MONO) found no statistically significant differences between the two groups over time. Differences between groups were non-significant at all time points, except for time point T3, where "CAP to AIR" values of monocytes (MONO) (M = 8, Range = 6) were significantly higher than "AIR to CAP" values (M = 6, Range = 6)(test = 95.500, p = 0.004) [Figure 6A]. Similarly, analysis of morning CORTISOL levels in blood samples indicated no statistically significant differences between the groups over time. Still, a statistically significant difference was observed between groups at time point T3, where "CAP to AIR" values of CORTISOL (M = 8.75, Range = 13.78) were significantly lower than "AIR to CAP" values (M = 12.56, Range = 10.99) (test = 311.000, $p = 0.002$). The same difference was borderline non-significant at the end of the follow-up period at 10-11 weeks (T4; MW = 311.000, $p = 0.023$) [Figure 6B].

Differences were also observed across time of MCVfl, mainly in the "AIR to CAP" group. Specifically, a borderline non-statistically significant increase was observed in the values of MCVfl between baseline (M=90.85, Range =11.50) and the end of the study at T4 (M=91.95, Range =10.00) for the "AIR to CAP group" (test =12.600, p=0.013) [Figure 6C]. In contrast, a statistically significant decrease was observed in the values of ferritin (FERR) between baseline (M=89.30, Range = 452.80) and T4 (M = 68.05, Range = 353.50) for the "CAP to AIR " group (test = 12.900, $p = 0.002$) [Figure 6D]. And a similar but non-significant change for the "AIR to CAP group" (test = 10.620, p = 0.014/ 0.009. A decrease was also observed for Na (test = 14.740, p = 0.002 with baseline Na (M = 142.00, Range = 9.90) (T1) and the end of the study (T4) (M = 140.00, Range = 10.00) [Figure 6E]. Finally, a trend toward differences between T1 and T2 compared with T3 and T4 was observed in the "AIR to CAP" group, with Prolactin (PRL) values ranging from 0.020 to 0.042, with higher PRL at T3 and T4 than at baseline (T1) and T2. Moreover, a statistically significant interaction effect was observed (χ^2 = 1,899, $p < 0.001$), indicating that, in the "AIR to CAP" group, the increase at T2 was maintained through the end of follow-up. In contrast, in the "CAP to AIR" group, the increase is observed at T3 and remains high till the end of the study (T4) [Figure 6F]. Statistically significant interaction effects were also found for triglycerides (TRG) [Figure 3G] and CA (calcium) [Figure 6H]. Specifically regarding TRG and based on the multiple comparisons test (test = 3,299, p = 0,022) the "AIR to CAP" group shows a decrease at T2 that is retained up to the end of the follow up with a slight increase at T4, while in the "CAP to AIR" an increase is observed at T2 only followed by a decrease at T3 until the end of the study (T4) [Figure 3G]. A similar pattern is observed for CA values (test = 3,245, $p = 0.023$), with a minor decrease at T3 in the "CAP to AIR" group [Figure 6H]. The indicators are currently co-evaluated for clinical relevance alongside BIA, salivary cortisol levels over 24 h, and condition-specific questionnaire analyses.

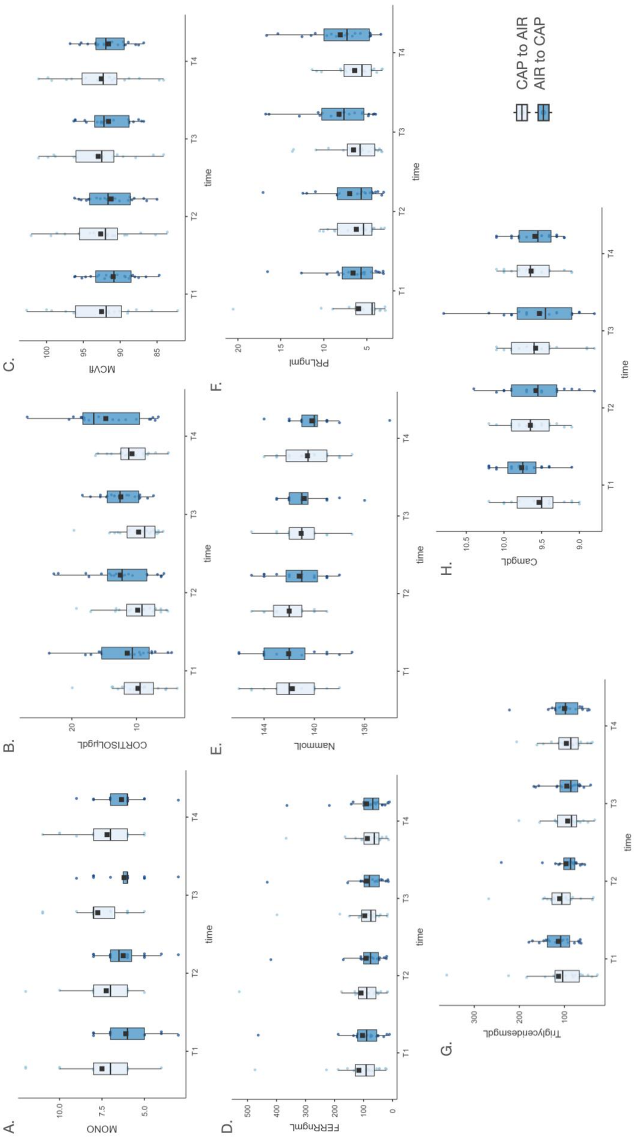


Figure 6. Changes over time (T1 to T4) in hematological, biochemical, and endocrinological indicators and biomarkers depicted as comparisons amongst Group A (CAP to AIR) and Group B (AIR to CAP) participants. A. MONO, B. CORTISOL-Blood Cortisol, C. MCVfl, D. FERR (Ferritin), E. NA (Na, sodium) F. PRL (Prolactin), G.Triglycerides (TRG), G. CA (Ca, Calcium).

DISCUSSION

In the modern world, population aging is a common sociological phenomenon. Despite this, a growing number of individuals aspire to age well, remain active, and extend their life expectancy by a few healthy years. Because of their age, individuals face deteriorating physiological and mental functions, which lead to a decreased sense of well-being and an increased risk of developing cerebrovascular and cardiovascular disease, diabetes, or neurodegeneration. More importantly, well-being, particularly among older adults, is critical for nurturing physical and mental health and improving QoL[29-30]. Subjective well-being is frequently used to assess overall quality of life in healthy[29] and ailing individuals[3,31-32]. Physical health, mental health, living environment, social phenomena, and lifestyle factors all affect subjective well-being. Thus, personalized treatments that improve quality of life will become part of everyday life in the years to come[20].

Extended periods of stressful life events modify the immune system, metabolism, and activate inflammatory pathways, hampering cell senescence and function[33], leading to a variety of medical and mental illnesses, including depression, cancer, metabolic syndrome, and cardiovascular disease[34-37]. Stressful life events can affect individuals' behavior at work, including reduced workplace involvement, decreased performance effectiveness, decreased job satisfaction, and, ultimately, absenteeism, tardiness, and turnover[38-39]. Stressful life events lead to workforce stress, illness, and, subsequently, poorer QoL[40-45].

Persistent environmental stressors lead to several chronic symptomatic diseases. The most prominent appears to be fibromyalgia, a clinical entity defined by the presence of chronic widespread pain, fatigue, poor sleep, and cognitive disturbances. These symptoms are common and nonspecific, and they vary not only among patients but also within the same patient over the course of the disease. The goal of the therapy is to reduce pain and fatigue and encourage patients to become more physically active through a multimodal, tailored approach that integrates education, exercise, and cognitive-behavioral therapy. The goal of the treatment is to reduce pain and encourage patients to become more physically active through a multimodal personalized therapeutic plan that incorporates education, exercise, cognitive-behavioral techniques, and drugs. Responses to existing therapeutic approaches vary widely: some patients respond effectively, whereas others appear to derive little long-term benefit[13]. Having analyzed clinical data collected from patients who survive a stressful infection, it is becoming increasingly evident that the health impact of COVID-19 goes beyond the period of viral incubation; with 63% of patients reporting persistent symptoms such as fatigue and “brain fog” to be the most common, symptoms that coexist with “long COVID”[15] and adrenal insufficiency[14-15]. Recently, it was first reported that fatigue following COVID-19 was not attributable to overt adrenal impairment[15]. Then, the persistence of symptoms and their effects on QoL in persons who had COVID-19 one year after admission, as well as the impact of systemic corticosteroid treatment during the acute phase of the illness, were analyzed for “bodily pain” and “mental health”. Most symptoms were less frequent in the group that received corticosteroids, with statistically significant differences for headache, dysphagia, chest pain, and depression. Corticosteroids administered during the acute phase of COVID-19 may improve patients’ quality of life and reduce long-term symptoms[46]. Consequently, developing innovative non-invasive physical therapies to alleviate the negative impact of stressors could be a one-way path towards the amelioration of chronic pain, fatigue, sleep disorders, and Long-COVID syndrome, leading to the improvement of the QoL of patients in Europe.

It cannot be excluded that CAP has minimal adverse effects at the molecular level; these remain the subject of ongoing analysis, but results to date suggest that the substantial benefits of CAP outweigh any unproven adverse effects[17-18]. Current studies on cell culture and animal models are more accessible and easier to conduct; however, expanded analysis of CAP effects in disease and regenerative medicine studies in human patients would be of major benefit. Evidently, the Human Regenerator Power Jet, as a direct, air-based, user-interactive CAP+ -generating electronic bed device for the whole body, provides for the active involvement of the user in the discharge configuration, and, due to its electrical self-limitation, is suitable for both wellness and presumptive targeted medical applications aimed at improving QoL worldwide[20]. Its use as supportive care to expedite medical interventions is expected to advance the therapeutic process toward a less invasive and distressing experience for patients, while also significantly reducing the financial burden of existing treatments worldwide.

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Authors’ contributions

Conceived and designed the study, analyzed and interpreted the data, critically reviewed the intellectual content, accuracy, and integrity of the results, and wrote the manuscript: E.R and G.P.C;
Analyzed and interpreted the data: N.A;
Data acquisition: E.R, A.M, and E.P;
All authors approved the article version for publication.

Availability of data and materials

The research results will be published in peer-reviewed articles in high-impact journals.

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Conflict of interest

All authors declared that there are no conflicts of interest in this work.

Ethical approval and consent to participate

The HR-QoL clinical study was conducted in accordance with the Declaration of Helsinki[47]. The clinical protocol was approved by the Institutional Ethics Committee of the University Research Institute for the Study of Genetic & Malignant Disorders in Childhood (renamed Maternal and Child Health and Precision Medicine), School of Medicine, NKUA (RPURI9023/10.04.2024). Privacy and data confidentiality were ensured by GDPR-compliant forms for the HR-QoL study, which were signed by participants at both the Endocrine Unit (NKUA) and at the Corpus Regen Wellness Center (Athens). The HR-QoL study is registered on ClinicalTrials.gov under NCT07279272 (US). All participants were fully informed that a) their participation was entirely voluntary and that b) they could unconditionally withdraw from the study at any time. Consent Forms for the participation in the Clinical Study were completed at the Endocrine Unit (NKUA).

Consent for publication

Not applicable.

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