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Impact of Hyperbaric Oxygen Therapy on Physical and Cognitive Frailty in Community- Dwelling Older Adults: A Retrospective Observational Study

Dr. Eleni Margioti

eleni@braindubai.ae

The Brain & Performance Centre by DP World

Dr. Akyllina Despoti

The Brain & Performance Centre by DP World

Suzette Van Wyk

The Brain & Performance Centre by DP World

Fatma Alsayegh

The Brain & Performance Centre by DP World

Leen Farah

The Brain & Performance Centre by DP World

Rabbia Basharat

The Brain & Performance Centre by DP World

Taif Al Delamie

The Brain & Performance Centre by DP World

Sadaf Tanveer

The Brain & Performance Centre by DP World

Megha Narayan

The Brain & Performance Centre by DP World

Marah Odeh

The Brain & Performance Centre by DP World

Dr. Zemer Wang

The Brain & Performance Centre by DP World

Dr. Gil Suzin

Sagol Centre for Hyperbaric Medicine and Research, Shamir (Assaf Harofeh) Medical Center

Dr. Amir Hadanny

Sagol Centre for Hyperbaric Medicine and Research, Shamir (Assaf Harofeh) Medical Center

Dr. Shai Efrati

Sagol Centre for Hyperbaric Medicine and Research, Shamir (Assaf Harofeh) Medical Center

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Abstract

Background:

Age-related declines in physical performance and cognitive functioning are well-documented in gerontological research and are closely linked to increased vulnerability to frailty. Frailty is now conceptualized as a multifactorial clinical syndrome marked by reduced physiological reserve, diminished resilience to stressors, and heightened risk of functional and cognitive deterioration. In parallel with growing interest in non-pharmacological strategies to mitigate age-associated decline, hyperbaric oxygen therapy (HBOT) has emerged as a potential intervention with biological mechanisms capable of influencing both cognitive and physical domains. The potential role of HBOT in modulating neuroplasticity, improving oxygenation, and enhancing tissue repair has led to a renewed focus on its use in aging populations.

Methods:

The study sample consisted of older adults participating in the HBOT program at the Brain and Performance Centre in Dubai (mean age 69.4 ± 8.3 years; 87.3% male). Data were extracted retrospectively from clinical records in a pre–post observational design. Physical frailty was defined using a modified Fried phenotype model, whereby individuals meeting three or more criteria were classified as frail, and those meeting one or two criteria as pre-frail, and those meeting none as non-frail. Cognitive frailty was identified when physical frailty co-occurred with mild cognitive impairment, operationalized as performance falling more than 1.5 standard deviations below age-, gender-, and education-adjusted norms on the NeuroTrax Global Cognitive Score, excluding individuals with dementia. Continuous variables were summarized using means and standard deviations; categorical variables were reported as frequencies and percentages. Pre–post differences were assessed using chi-square or Fisher's exact tests for categorical outcomes and the Wilcoxon signed-rank test for continuous measures.

Results:

A total of 63 cognitively intact older adults were included in the final analysis. At baseline, 73.7% of participants were categorized as pre-frail, while 22.8% met criteria for frailty. Post-intervention analyses indicated a marked shift, with the proportion classified as frail decreasing to 8.8%, and the rate of pre-frailty rising to 89.5%. This reduction in physical frailty prevalence was statistically significant ($p = 0.040$). Cognitive frailty also declined considerably, from 14.5% to 1.8%, representing a statistically significant reduction following the intervention ($p = 0.016$). Statistically significant improvements were observed in cognitive performance (MoCA and NeuroTrax), walking speed, grip strength, and overall physical activity levels. Participants additionally demonstrated reductions in body mass index, whereas skeletal muscle mass remained stable. Self-reported cognitive concerns decreased from 63.5% to 23.8% ($p < 0.001$), and

reports of high energy levels increased from 42.6% to 77.8% (p = 0.001), suggesting meaningful subjective benefits.

Conclusion:

The findings provide preliminary evidence that HBOT may contribute to substantial reductions in both physical and cognitive frailty among older adults. The observed improvements are consistent with biological pathways known to influence age-related functional decline, including enhanced oxygen utilization, vascular responsiveness, and potential neuroplastic mechanisms. Although these results are encouraging, they should be interpreted as early evidence. Larger, controlled studies are warranted to establish causality, clarify underlying mechanisms, and determine the durability of the observed benefits. Nevertheless, HBOT appears to represent a promising non-pharmacological option for promoting healthier aging and supporting functional independence.

Clinical trial registration

Clinical trial number: not applicable. This was a retrospective observational study using routinely collected clinical data.

Introduction

The global population is undergoing a profound demographic shift, with the proportion of adults aged 65 years and older rising more rapidly than at any time in recorded history. Current projections estimate that by 2050, more than two billion individuals will be over 80 years old (Kastner et al., 2019; Lunenfeld & Stratton, 2013). This unprecedented expansion of the older population has sharpened the focus on conditions that undermine independence and quality of life, particularly frailty and cognitive decline, two issues increasingly recognized as central public health challenges in aging societies (Murray & Lopez, 2013).

Frailty itself is conceptualized as a multidimensional clinical syndrome reflecting diminished physiological reserve and increased vulnerability to even minor stressors. It emerges from the gradual accumulation of deficits across multiple biological systems (Fried et al., 2001; Clegg et al., 2013) and is associated with elevated risks of falls, disability, hospitalization, and mortality. Although widely studied, frailty still lacks a single universally endorsed definition. Much of the field is shaped by two influential theoretical models. The first is Fried and colleagues' frailty phenotype, which operationalizes frailty through five criteria: unintentional weight loss, muscle weakness, exhaustion, slowed gait, and low activity levels, classifying individuals as frail when three or more criteria are present (Fried et al., 2001). The second is the deficit accumulation model proposed by Mitnitski, Mogilner, and Rockwood (2001), which views frailty as a cumulative index of age-related health deficits that may include comorbidities, functional impairments, cognitive difficulties, and psychosocial vulnerabilities (Gobbens et al., 2010; de

Vries et al., 2011). Prevalence estimates vary substantially across studies of community-dwelling older adults aged 65 years and above, generally ranging between 4% and 22% (Avila-Funes et al., 2008; Collard et al., 2012; Song et al., 2010).

Within this broader framework, the concept of cognitive frailty has received increasing attention. Cognitive frailty describes the co-occurrence of physical frailty and mild cognitive impairment (MCI), in the absence of dementia, and is associated with markedly higher risks of disability, neurodegenerative progression, institutionalization, and mortality (Kelaiditi et al., 2013; Robertson et al., 2013). Large-scale population-based evidence further supports a close association between subjective cognitive decline and physical frailty, highlighting the early interplay between cognitive vulnerability and systemic physiological decline (Margioti et al., 2020). Importantly, both physical and cognitive frailty appear to be at least partially modifiable, especially when identified early. Shared biological mechanisms including chronic inflammation, oxidative damage, mitochondrial dysfunction, vascular compromise, and impaired tissue repair contribute to both physical vulnerability and cognitive decline (Clegg et al., 2013). This overlap underscores the need for interventions capable of targeting these age-related pathways in an integrated manner.

Hyperbaric oxygen therapy (HBOT) has recently emerged as a potential therapeutic modality with relevance to these mechanisms. HBOT involves the intermittent inhalation of 100% oxygen at pressures exceeding one atmosphere absolute, substantially elevating tissue oxygenation. Repeated exposures induce a physiological process often described as the “hyperoxic–hypoxic paradox,” whereby controlled fluctuations in oxygen levels activate hypoxia-inducible factor 1-alpha (HIF-1α) and related signalling cascades. These pathways regulate angiogenesis, neurogenesis, mitochondrial biogenesis, and anti-inflammatory responses (Hadanny & Efrati, 2020). As a result, HBOT has been associated with enhanced vascular endothelial growth factor (VEGF) activity, increased stem cell mobilization, and improved microvascular perfusion changes that may be particularly relevant in the context of age-related decline (Hadanny & Efrati, 2020; Hachmo et al., 2020).

A growing body of clinical evidence supports the potential of HBOT to counteract both cognitive and physical aspects of aging. For example, Hadanny et al. (2020) reported significant improvements in executive functions, attention, and processing speed following a 60-session HBOT protocol in cognitively healthy older adults, accompanied by measurable increases in cerebral perfusion. Parallel findings from Hadanny et al. (2024) demonstrated gains in aerobic capacity (VO_2max) and myocardial perfusion in sedentary older adults, suggesting that HBOT may also influence cardiovascular and musculoskeletal systems implicated in physical frailty. Mechanistic studies have further documented enhanced mitochondrial respiration, reductions in cellular senescence, increased telomere length, and decreased accumulation of senescent cells after HBOT (Hachmo et al., 2020; Hadanny et al., 2022). Together, these findings indicate that HBOT may interact with several fundamental hallmarks of biological aging.

Given the absence of approved pharmacological treatments for frailty and the limited long-term efficacy of conventional lifestyle-based approaches (Clegg et al., 2013), HBOT presents a compelling systems-

level intervention. By simultaneously modulating inflammation, oxygenation, vascular function, and mitochondrial capacity, HBOT may address the interconnected pathophysiological processes underlying both physical and cognitive frailty.

In this study, we investigated the effects of a three-month HBOT protocol on physical and cognitive frailty in community-dwelling older adults. We hypothesized that participation in HBOT would lead to measurable improvements in cognitive performance, key physical indicators such as gait speed and grip strength, and subjective perceptions of memory and energy. Correspondingly, we anticipated a reduction in the prevalence of both physical frailty and cognitive frailty following the intervention.

Method

Participants and intervention

Participants were recruited from a cohort enrolled in the healthy aging program at the Brain and Performance Centre in Dubai. This was a retrospective pre–post observational study without a control group. The initial screening pool included 244 adults, from which several exclusion criteria were applied to create a more homogeneous sample of cognitively intact, community-dwelling older individuals. Participants were excluded if they had a documented history of neurodegenerative disease, post-COVID condition, traumatic brain injury, cerebrovascular stroke, or clinically diagnosed anxiety or depressive disorders. To align the sample with the study's focus on aging, only adults aged 60 years and older were retained. Following these steps, the final analytic sample consisted of 63 older adults (mean age = 69.4 ± 8.3 years), the majority of whom were male (87.3%). All procedures were conducted in accordance with relevant ethical guidelines, and all participants provided written informed consent. All participants provided written informed consent for clinical assessment and treatment before joining the programme. DSREC waived the requirement for additional informed consent for the retrospective review of their clinical records.

Each participant completed a minimum of 60 HBOT sessions over a 12-week treatment period. Sessions were conducted in a multi-place hyperbaric chamber, in which participants inhaled 100% oxygen at 2.0 atmospheres absolute (ATA) for approximately 90 minutes per session. To reduce the risk of oxygen toxicity, 5-minute air breaks were incorporated every 20 minutes of oxygen breathing. These intermittent air breaks create fluctuations in tissue oxygen levels and are considered a key component of the protocol, contributing to the hyperoxic–hypoxic paradox (HHP), a physiological mechanism believed to activate hypoxia-related cellular pathways despite hyperoxic exposure (Efrati & Ben-Jacob, 2014; Hadanny & Efrati, 2020).

Treatment was delivered five days per week and followed standardized HBOT protocols previously demonstrated to be safe and effective for older adult populations (Efrati et al., 2013). Comprehensive baseline assessments were carried out immediately before the first HBOT session, and all measures were repeated at the conclusion of the program to evaluate changes in physical frailty, cognitive

performance, and subjective symptoms. Additionally, the participants were concurrently participated in a comprehensive, multidisciplinary program throughout the intervention period. In addition to HBOT, they received interventions tailored to their clinical needs, including cognitive training, supervised physical exercise or strength training, physiotherapy, nutritional guidance, and ongoing medical monitoring by physicians.

Cognitive assessment

Cognitive functioning was assessed using the NeuroTrax computerized cognitive battery, with the Global Cognitive Score serving as the primary performance-based measure for the operationalisation of cognitive frailty (defined as ≥ 1.5 standard deviations below age-, gender-, and education-adjusted norms). The Montreal Cognitive Assessment (MoCA) was also administered as a brief screening tool to characterise general cognitive status and monitor global cognitive change, but it was not used to determine cognitive frailty classification.

Definition of physical frailty

Physical frailty was assessed using a modified version of the Fried frailty phenotype (Fried et al., 2001), adapted to align with the clinical metrics and biometric indicators available in the study database. The phenotype includes five components: slowness, shrinking/weight loss, exhaustion, low physical activity, and weakness, each scored dichotomously (1 = present, 0 = absent). Total scores ranged from 0 to 5 and were used to classify participants as non-frail (0), pre-frail (1–2), or frail (3–5). All criteria were measured at baseline and again following the HBOT intervention. The operational definitions applied in this study were as follows:

1. Slowness (Mobility): Mobility was evaluated using an 8–10-meter walking test. Participants whose walking speed fell within the slowest 20% of the sample based on test completion time were coded as meeting the slowness criterion. This threshold reflects clinically meaningful reductions in functional mobility.
2. Shrinking / Weight Loss: Shrinking was defined using a Body Mass Index (BMI) cutoff of < 18.5 kg/m^2, indicating clinically significant reductions in body mass and a potential marker of sarcopenia-related frailty.
3. Exhaustion (Low Endurance): Exhaustion was determined through self-reported descriptions of energy levels collected during neuropsychological interviews. Responses were coded qualitatively as “high” or “low,” integrating both participant self-report and clinical judgment. Reports of persistently low or declining energy were coded as meeting the exhaustion criterion.

4. Low Physical Activity: Physical activity levels were quantified using SECA-derived Physical Activity Level (PAL) classifications. Participants with gender-matched PAL values in the lowest 20% of the sample were categorized as having low physical activity. In borderline cases, clinical judgment was applied to ensure accurate classification.
5. Weakness: Weakness was assessed using electronic hand dynamometry to measure dominant-hand grip strength. Individuals in the lowest 20% of grip-strength values for their gender and BMI category were coded as meeting the weakness criterion, a widely validated indicator of diminished muscular function.

A summary of the correspondence between the five Fried frailty phenotype components and the clinical measures used in the present study is presented in Table 1.

Table 1
Mapping of Fried Frailty Phenotype criteria to clinical measures used in the present study

Frailty Component	Conceptual Definition (Fried et al., 2001)	Measurement Method	Operational Definition
Slowness	Reduced gait speed reflecting impaired mobility	8–10 m walk test	Participants within the slowest 20% of the study sample based on walking time
Shrinking (Weight Loss)	Unintentional weight loss or reduced body mass	Body Mass Index (BMI)	BMI < 18.5 kg/m²
Exhaustion	Self-reported fatigue or reduced endurance	Self-reported energy level during clinical interview	Participants reporting persistently low energy levels
Low Physical Activity	Reduced engagement in habitual physical activity	SECA-derived Physical Activity Level (PAL)	Participants within the lowest 20% of gender-matched PAL values
Weakness	Reduced muscular strength	Hand grip strength measured using electronic dynamometer	Participants within the lowest 20% of grip strength values stratified by gender and BMI

Note. Each frailty component was scored dichotomously (0 = absent, 1 = present). Total scores ranged from 0 to 5 and were used to classify participants as non-frail (0), pre-frail (1–2), or frail (3–5) according to the modified Fried frailty phenotype framework.

Frailty status was calculated by summing the number of criteria met, yielding a total score from 0 to 5. Changes in individual criteria from baseline to post-HBOT were examined to evaluate improvements or worsening in frailty severity. A reduction in the number of criteria present after treatment was interpreted as a decrease in overall frailty burden, consistent with established applications of the Fried model (Fried et al., 2001).

Definition of cognitive frailty

The International Consensus Group defines cognitive frailty as the co-occurrence of physical frailty and cognitive impairment, typically operationalized by a Clinical Dementia Rating (CDR) score of 0.5 in the absence of dementia (Kelaiditi et al., 2013). Although widely used, the CDR is designed primarily to detect clinically manifest impairment and may not capture early or subtle cognitive changes in generally healthy older adults. As reported in previous studies, cognitive impairment has also been operationalized using performance-based neuropsychological criteria when CDR scores are unavailable or insufficiently sensitive (Robertson et al., 2013). Accordingly, in the present study, cognitive impairment was defined using a performance-based criterion of ≥ 1.5 standard deviations below age- and education-adjusted norms, operationalized through the Global Cognitive Score of the Neurotrax computerized cognitive battery. This approach was selected to ensure adequate sensitivity for detecting subtle cognitive changes in a prevention-focused cohort without clinically diagnosed cognitive impairment.

Therefore, cognitive impairment in the present study was operationalized using a performance-based neuropsychological criterion rather than CDR scoring (Ruan et al., 2015; Sugimoto et al., 2018). Cognitive frailty was defined by the presence of both:

1. Physical frailty: Classification as pre-frail or frail based on the modified Fried phenotype.
2. Objective cognitive impairment: A Global Cognitive Score on the NeuroTrax computerized battery falling ≥ 1.5 standard deviations below age-, gender-, and education-adjusted normative values.

Participants were classified as cognitively frail only if both criteria were met, provided they remained independent in instrumental activities of daily living (IADLs) and did not meet diagnostic criteria for dementia. Cognitive frailty status was assessed at baseline and reassessed following completion of the HBOT protocol. Improvement in cognitive frailty diagnosis was defined as no longer meeting the combined criteria of physical frailty and objective cognitive impairment used at baseline.

Statistical analysis

Descriptive statistics were used to characterize the study sample and to summarize all outcome variables. Continuous measures, including gait speed, grip strength, and cognitive performance indices, were reported as means and standard deviations (SD). Categorical variables, such as frailty status and the presence of subjective cognitive complaints, were expressed as frequencies and percentages.

To examine the effects of the HBOT intervention, paired comparisons were conducted between baseline and post-treatment assessments. Changes in categorical outcomes (e.g., frailty and cognitive frailty prevalence) were evaluated using McNemar’s chi-square test, with Fisher’s exact test applied when expected cell counts were insufficient to meet chi-square assumptions. For continuous or ordinal variables assessed at two time points, within-subject differences were analysed using the Wilcoxon signed-rank test. The Wilcoxon signed-rank test was selected due to the non-parametric nature and skewed distributions of several functional outcomes (e.g., walking speed and grip strength), making it

more appropriate than parametric paired tests. All statistical tests were two-tailed, with significance set at $p < 0.05$. Analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). No formal correction for multiple comparisons was applied due to the exploratory nature of the study; therefore, results should be interpreted cautiously.

Results

A total of 63 cognitively intact older adults were included in the final analysis. The mean age of the cohort was 69.4 years (SD = 8.3), and the sample was predominantly male (87.3%). Educational backgrounds varied, with 39.7% of participants holding a bachelor's degree, 25.4% a master's degree, and 14.3% a doctoral qualification. The group was culturally heterogeneous: 42.9% originated from Gulf countries such as the United Arab Emirates, Saudi Arabia, Kuwait, Bahrain, Qatar, and Oman. Most participants were married (90.5%), and two-thirds (66.7%) reported living with or cohabiting with a spouse or partner at the time of the assessment. A full overview of demographic characteristics is presented in Table 2.

Baseline frailty classifications derived from the modified Fried phenotype showed that 3.5% of participants were non-frail, 73.7% were pre-frail, and 22.8% met full criteria for frailty (Table 3). After completing the HBOT protocol, a notable shift in distribution was observed. The proportion of individuals classified as frail declined significantly to 8.8%, while the majority of participants (89.5%) fell within the pre-frail range. A small percentage (1.8%) met criteria for non-frailty at post-intervention assessment. The distribution of physical and cognitive frailty classifications at pre- and post-intervention is illustrated in Fig. 1.

Among participants classified as pre-frail or frail at baseline, the prevalence of cognitive frailty decreased markedly from 14.5% prior to HBOT to 1.8% following treatment. This reduction represents a statistically significant improvement in the combined physical and cognitive dimensions of vulnerability. Cognitive frailty analyses were restricted to individuals meeting criteria for pre-frailty or frailty in physical status at each time point; consequently, the number of participants included differed between pre- and post-intervention assessments, accounting for minor discrepancies in totals.

To illustrate individual-level changes in frailty status, a shift visualization (Sankey diagram) was generated (Fig. 2). The diagram demonstrates movement of participants toward less severe frailty states from pre- to post-intervention. Many individuals categorized as physically frail at baseline transitioned to the pre-frail category after treatment, while cognitive frailty also declined markedly, with most participants no longer meeting criteria post-intervention.

Further analyses of continuous outcome measures are presented in Table 4a. The HBOT intervention was associated with notable improvements across several cognitive, physical, and subjective health indicators. Cognitive performance demonstrated a clear upward shift, with significant increases observed in both Montreal Cognitive Assessment (MoCA) scores (23.9 ± 3.2 to 24.5 ± 2.9, $p < 0.001$) and the NeuroTrax Global Cognitive Score (97.9 ± 9.9 to 102.2 ± 8.9, $p < 0.001$). These gains suggest

enhanced functioning in multiple cognitive domains, including attention, memory, and executive processes. Changes in body composition also emerged, with participants exhibiting a significant reduction in Body Mass Index (BMI) (27.2 ± 3.1 to 26.6 ± 2.6, $p < 0.001$), while Skeletal Muscle Mass remained essentially unchanged. Functional measures reflected similarly positive trends: physical activity levels increased (1.4 ± 0.1 to 1.5 ± 0.1, $p < 0.001$), walking speed improved (median 4.2 to 3.8 seconds, $p < 0.001$), and grip strength rose in both the dominant (30.6 ± 12.0 to 34.0 ± 11.4 kg, $p < 0.001$) and non-dominant hands (30.4 ± 11.3 to 31.5 ± 11.1 kg, $p < 0.001$).

To further explore outcomes in the subgroup with baseline cognitive frailty, Table 4b presents changes in health characteristics before and after the intervention for the eight participants initially categorized as cognitively frail. MoCA, physical activity, and right-hand grip strength showed significant increases ($p = .018$, $p = .020$, and $p = .030$, respectively). The General Cognitive Score on NeuroTrax, left-hand grip strength, and Skeletal Muscle Mass also increased; however, these changes did not reach statistical significance ($p = .219$, $p = .176$, and $p = .219$, respectively). BMI and 8/10-meter walk time also did not change significantly ($p = .879$ and $p = .392$, respectively). Moreover, after the intervention, the percentage of those who believed they were forgetful was significantly lower than before (25% vs. 100%, respectively). Notably, all participants in the cognitively frail subgroup reported improved energy levels following the intervention, shifting from 100% reporting low energy at baseline to 100% reporting high energy post-treatment.

Improvements also extended to subjective cognitive complaints in the overall sample. Based on responses to a structured self-report item (“Do you believe that you forget?”), the proportion of participants endorsing cognitive concerns decreased significantly from 63.5% at baseline to 23.8% following treatment ($p < 0.001$). In addition, self-reported energy levels improved substantially. Based on responses to a subjective energy-level question (categorised as low energy vs high energy), the proportion of participants reporting high energy levels increased from 42.6% at baseline to 77.8% following the intervention. These findings indicate consistent and clinically meaningful improvements in subjective and objective cognitive performance, physical function, and energy levels following completion of the HBOT protocol.

Table 2
Sample's characteristics

		N	%
Gender	**Female**	**8**	**12.7**
	Male	**55**	**87.3**
Age, Mean (SD), Median (IQR)		69.4 (8.3)	67.0 (63–75)
YoE, Mean (SD), Median (IQR)		16.9 (3.6)	16.0 (15–19)
HBOT Prescribed, Mean (SD), Median (IQR)		60.3 (2.5)	60 (60 — 60)
HBOT Scheduled, Mean (SD), Median (IQR)		72.4 (16.7)	64 (61 — 79)
HBOT Executed, Mean (SD), Median (IQR)		62.2 (16)	62 (60 — 69)
Educational level	Associate degree	4	6.3
	Bachelor's degree	25	39.7
	Graduate Degree (MA)	16	25.4
	Graduate Degree (PhD)	9	14.3
	High school	1	1.6
	High school or equivalent	5	7.9
	Less than high school	1	1.6
	No Degree	1	1.6
	Some College education but no degree	1	1.6
Arab Ethnicity	No	36	57.1
	Yes	27	42.9
Marital Status	Divorced	6	9.5
	Married	57	90.5
Current life partner	No	21	33.3
	Yes	42	66.7

Table 3
Physical and cognitive frailty pre- and post-intervention

		Pre		Post		P
		N	%	N	%	
Physical Frailty	No (non-frail/pre-frail)	44	77.2	52	91.2	0.040
	Yes (frail)	13	22.8	5	8.8	
Cognitive Frailty*	No	47	85.5	55	98.2	0.016
	Yes	8	14.5	1	1.8	

*Calculated on those categorized in the pre-frail or frail stage of physical frailty

Table 4
a. Comparison of participants' characteristics before and after intervention

		Pre		Post		P
		Mean (SD)	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**	
MoCA		23.9 (3.2)	24 (22 – 27)	24.5 (2.9)	25 (22 – 27)	< 0.001
General Cognitive Score on NeuroTrax		97.9 (9.9)	99.8 (94.4 – 105.7)	102.2 (8.9)	103.1 (96.9 – 108.7)	< 0.001
BMI		27.2 (3.1)	27 (25.3 – 28.7)	26.6 (2.6)	26.5 (25.5 – 27.6)	< 0.001
Skeletal Muscle Mass		24.4 (5.1)	25.3 (21.2 – 27.4)	24.2 (4.9)	24.9 (21.9 – 27.2)	0.517
Physical Activity		1.4 (0.1)	1.4 (1.4 – 1.5)	1.5 (0.1)	1.5 (1.4 – 1.5)	< 0.001
Walking speed		5 (3.5)	4.2 (3.5 – 5.2)	4.4 (2.6)	3.8 (3.4 – 4.2)	< 0.001
Grip strength right hand		30.6 (12)	29.2 (22.3 – 36.7)	34 (11.4)	33.2 (26.7 – 42)	< 0.001
Grip strength left hand		30.4 (11.3)	29.5 (25.7 – 35)	31.5 (11.1)	31.5 (26.7 – 39)	< 0.001
		N	**%**	**N**	**%**	
Subjective Cognitive Complaint Question: "Do you believe that you forget?"	No	23	36.5	48	76.2	< 0.001
	Yes	40	63.5	15	23.8	
Subjective Question regarding energy level	Low energy	31	57.4	12	22.2	0.001
	High energy	23	42.6	42	77.8	

Table 4

b. Comparison of characteristics before and after intervention for the 8 participants that had been categorized as having cognitive frailty in the first assessment.

		Pre		Post	
		Mean (SD)	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**
MoCA		21.9 (2.7)	23 (19 – 24)	22.9 (2.3)	23.5 (20.5 – 24.5)
General Cognitive Score on NeuroTrax		93.8 (11.5)	97.9 (89–100.3)	97.7 (12.7)	99.4 (87.8–108.7)
BMI		26.3 (1.6)	26.3 (25.2 – 27)	26.2 (0.8)	26.2 (25.6 – 27)
Skeletal Muscle Mass		22.8 (4.1)	24.1 (21.7 – 25.6)	23.2 (3.7)	24.3 (22.8 – 25.6)
Physical Activity		1.5 (0.1)	1.5 (1.4 – 1.5)	1.6 (0.1)	1.5 (1.5 – 1.6)
8/10 Meter Walk		4.4 (1.9)	3.9 (3.1 – 4.9)	4.1 (0.9)	4 (3.4 – 4.3)
Grip strength right hand		23.9 (5)	22.7 (21.7 – 24.7)	27.4 (5.4)	29.2 (23.7 – 30)
Grip strength left hand		28.1 (5.1)	28.3 (25 – 32)	29.8 (5)	29.7 (29 – 33.3)
		N	**%**	**N**	**%**
Subjective Cognitive Complaint Question: "Do you believe that you forget?"	No	0	0.0	6	75.0
	Yes	8	100.0	2	25.0
Subjective Question regarding Energy Level	Low energy	8	100.0	0	0.0
	High energy	0	0.0	8	100.0

Note

The diagram illustrates individual participant transitions in both physical frailty and cognitive frailty status from pre- to post-intervention. Physical frailty (Yes/No) and cognitive frailty (Yes/No) were classified according to the study criteria. Flow widths are proportional to the number of participants following each transition pathway. Cognitive frailty was defined as the co-occurrence of physical frailty and cognitive impairment. Analyses include participants with complete pre–post data (n = 63).

Discussion

The findings provide preliminary but compelling evidence that HBOT may reduce both physical and cognitive frailty in community-dwelling older adults. Individuals who completed the three-month protocol demonstrated meaningful reductions in frailty severity, alongside improvements in cognitive performance (MoCA and NeuroTrax), mobility, handgrip strength, and self-reported energy and memory. Taken together, these effects are consistent with a growing body of research suggesting that HBOT may enhance resilience to age-related decline by acting on systemic, vascular, and neurobiological pathways involved in aging (Hadanny et al., 2020; Hadanny et al., 2024).

From a physical health perspective, improvements observed in walking speed, muscular strength, and perceived energy parallel physiological changes previously documented in older adults exposed to HBOT. For example, Hadanny et al. (2024) reported increases in VO_2 max, aerobic capacity, and myocardial perfusion in an age-comparable cohort. These findings are clinically important because slowed gait, muscle weakness, and low activity levels represent core components of the frailty phenotype (Fried et al., 2001; Chen et al., 2014). The observed pattern indicates that frailty severity was reduced following the intervention, as reflected by a decrease in the proportion of participants classified as frail and a corresponding increase in those classified as pre-frail. This shift suggests a transition toward less severe frailty states, rather than a direct return to robustness. Accordingly, the findings imply that the frail stage may be particularly responsive to intervention, with improvements manifesting as movement into the pre-frail category, which represents a more modifiable phase within the frailty continuum (Fried et al., 2001; Clegg et al., 2013; Morley et al., 2013). This pattern reflects a shift toward a more reversible stage of frailty, highlighting the potential window of intervention in pre-frail status. Among these mechanisms, mitochondrial function may represent a central pathway linking improvements across multiple organ systems.

The biological mechanisms associated with HBOT provide a coherent framework for interpreting the pattern of results observed in this study. HBOT, particularly through the hyperoxic–hypoxic paradox, induces controlled fluctuations in oxygen availability that activate hypoxia-inducible pathways and promote angiogenesis, neurogenesis, and anti-inflammatory responses (Hadanny & Efrati, 2020). These processes are associated with enhanced vascular function, improved oxygen utilization, and activity-dependent neuroplasticity, which may underlie the observed reductions in physical and cognitive frailty, as well as improvements in global cognitive performance, mobility, handgrip strength, and self-reported energy (Hadanny et al., 2024). Improved cerebral perfusion and metabolic efficiency may have contributed to gains in attention, memory, and executive functioning, while biological effects such as reduced inflammation and enhanced muscular oxygen delivery may underlie improvements in physical performance and frailty status (Hachmo et al., 2020; Hadanny et al., 2022).

At a cellular level, mitochondrial function may represent a central unifying mechanism linking these systemic effects. Mitochondrial dysfunction is widely recognized as a key contributor to aging, frailty, and reduced physiological resilience due to its essential role in energy production, oxidative stress

regulation, and tissue repair (López-Otín et al., 2013; Sun et al., 2016). HBOT has been shown to stimulate mitochondrial biogenesis, enhance oxidative phosphorylation efficiency, and improve cellular respiration, thereby supporting metabolic efficiency across multiple organ systems (Hadanny & Efrati, 2020). Together, these mechanisms suggest that HBOT may act on core biological mechanisms of aging, influencing both cognitive reserve and physical resilience.

Interestingly, body composition changes observed in the present study revealed a favorable shift. While Body Mass Index decreased significantly following the intervention, Skeletal Muscle Mass remained stable, suggesting that weight reduction was likely driven by decreases in fat mass and/or systemic inflammation rather than muscle loss. This finding is particularly noteworthy, as weight loss in older adults is typically associated with concomitant muscle loss and an increased risk of sarcopenia. This pattern may be conceptualized as a “sarcopenic paradox,” whereby weight reduction occurs without the expected decline in muscle mass. Such a shift reflects improved metabolic efficiency and inflammatory balance, both of which are closely linked to frailty reversal and healthier aging trajectories (Villareal et al., 2005; Batsis & Villareal, 2018; Cruz-Jentoft et al., 2019; Chen et al., 2014).

One important finding was the marked reduction in cognitive frailty, which declined from 14.5% at baseline to just 1.8% post-intervention. This substantial decrease highlights the dynamic and potentially reversible nature of cognitive frailty when targeted through multidomain physiological interventions that enhance both neural and systemic resilience (Kelaiditi et al., 2013). By improving cerebral perfusion, metabolic efficiency, and synaptic functioning, HBOT may contribute to strengthening cognitive reserve and reducing the risk of progression toward more advanced frailty stages, cognitive decline, or dementia. Notably, all participants who were categorized as cognitively frail at baseline (n = 8) reported improved energy levels following treatment, shifting from 100% reporting low energy before the intervention to 100% reporting high energy post-intervention. This change underscores the systemic nature of the observed improvements and suggests that HBOT may influence both cognitive and physiological vitality in individuals with combined cognitive and physical vulnerability.

Participants also reported significant improvements in subjective memory and vitality. While these outcomes may partly reflect increased engagement and expectancy associated with structured treatment participation, they remain clinically meaningful, as subjective cognitive decline is increasingly recognized as an early indicator and predictor of future cognitive impairment (Jessen et al., 2014). Enhanced memory, focus, and energy following HBOT may reflect improved functioning within neural networks involved in attention, executive control, and motivation (Hadanny et al., 2020). Furthermore, improvements in psychological well-being may facilitate greater engagement in physical, cognitive, and social activities, potentially initiating a positive feedback loop that supports healthier aging trajectories (Nguyen et al., 2021).

Limitations and Future Directions

Despite the encouraging results, several limitations must be considered when interpreting the findings of this study. First, the retrospective design and absence of a control or comparison group limit causal inference, making it difficult to determine the extent to which the observed improvements can be attributed specifically to HBOT rather than to nonspecific factors such as expectancy effects, regression to the mean, or concurrent lifestyle changes. In addition, participants were concurrently engaged in a multidisciplinary program, including nutritional guidance, physical exercise, physiotherapy, cognitive training, and ongoing medical support, which may have contributed to the observed outcomes. While the retrospective nature of this study precludes a definitive causal claim, the magnitude of change observed, particularly the substantial reduction in cognitive frailty (from 14.5% to 1.8%, representing an approximately 87% relative reduction), appears larger than would typically be expected from placebo effects or from the natural trajectory of frailty progression in aging populations. However, this interpretation should be approached with caution, as the effects of multimodal interventions cannot be disentangled within the current study design. Accordingly, these preliminary findings require confirmation in well-designed randomized controlled trials (RCTs) to establish the specificity, efficacy, and durability of HBOT-related effects on physical and cognitive frailty.

The sample's demographic composition presents an additional limitation. Because most participants were male, the generalizability of the findings is constrained. Prior research suggests that frailty trajectories and physiological responses to HBOT may differ by sex (Abellan van Kan et al., 2008), underscoring the importance of achieving greater gender balance in future prospective studies.

There are also methodological considerations. Frailty in the present study was assessed using the modified Fried phenotype, a well-established phenotypic approach focused on physical performance indicators. However, this framework does not capture other important dimensions of frailty. Future studies would benefit from adopting a multimodal frailty assessment, incorporating additional approaches such as deficit-accumulation indices, cognitive and functional measures, and biological markers (e.g., oxidative stress indices, and vascular function). Integrating these complementary domains would allow for a more comprehensive characterization of frailty and a deeper understanding of the mechanisms underlying observed changes. Likewise, while MoCA and NeuroTrax offered valuable indicators of cognitive status, the addition of neuroimaging or electrophysiological tools would allow for more direct characterization of neural adaptations associated with HBOT. Finally, the relatively high socioeconomic status of the sample, reflecting recruitment from a specialized brain health and performance clinic, may limit the generalizability of the findings to broader and more socioeconomically diverse populations.

Future research should prioritize rigorously designed, longitudinal randomized controlled trials to evaluate the specificity, durability, and mechanistic basis of HBOT-related improvements. Incorporating multimodal imaging techniques such as measures of cerebral perfusion, white matter integrity, or functional connectivity would advance understanding of the neurovascular pathways influenced by HBOT. Further work examining optimal treatment parameters, including session dosage, duration, and timing, as well as potential synergies with interventions such as aerobic exercise or cognitive training, is

warranted. Recruiting more diverse samples with balanced gender representation and broader ethnocultural backgrounds will also improve ecological validity and help identify sociocultural or demographic moderators of treatment response.

Conclusion

In conclusion, the findings of this study provide preliminary evidence that HBOT may contribute to reductions in both physical and cognitive frailty in older adults. The consistent pattern of improvements observed across cognitive, physiological, and subjective outcomes suggests that HBOT may impact shared biological pathways implicated in age-related decline. These results indicate that HBOT represents a promising non-pharmacological, multidomain approach for supporting healthier aging trajectories. While validation through controlled, randomised studies is required, the present findings highlight the potential of HBOT to enhance cognitive resilience, promote functional independence, and address key vulnerabilities associated with frailty in later life.

Declarations

Ethics approval and consent to participate

This study was approved by the Dubai Scientific Research Ethics Committee (DSREC), Dubai Health Authority, on 21 August 2026 (reference: DSREC-07/2026_32). All participants provided written informed consent for clinical assessment and treatment before joining the programme. DSREC approved a waiver of informed consent for the retrospective review of clinical records covering the period from 4 April 2021 to 1 March 2024. The study was conducted in accordance with the Declaration of Helsinki and applicable local requirements.

Conflict of Interest

The authors declare no competing financial or non-financial interests related to the conduct or reporting of this study. SE is shareholder in AVIV Scientific Ltd.

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Author Contribution

E.M. designed the study, analysed the data, and drafted the manuscript. A.D. and R.B. contributed to data collection and provided clinical input. S.V.W. contributed to data collection and patient assessments. F.A. contributed to data collection and clinical support. L.F. contributed to data extraction and handling. T.A.D., S.T., M.N., and M.O. supported data collection. Z.W. provided clinical oversight and study supervision. A.H. and S.E. provided study supervision. All authors reviewed and approved the final manuscript.

Data Availability

The datasets analysed during the current study are not publicly available to protect participant confidentiality. De-identified data are available from the corresponding author upon reasonable request, subject to institutional permission and applicable ethical and data protection requirements.

Clinical Trial Statement

Clinical trial number: not applicable.

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Figures

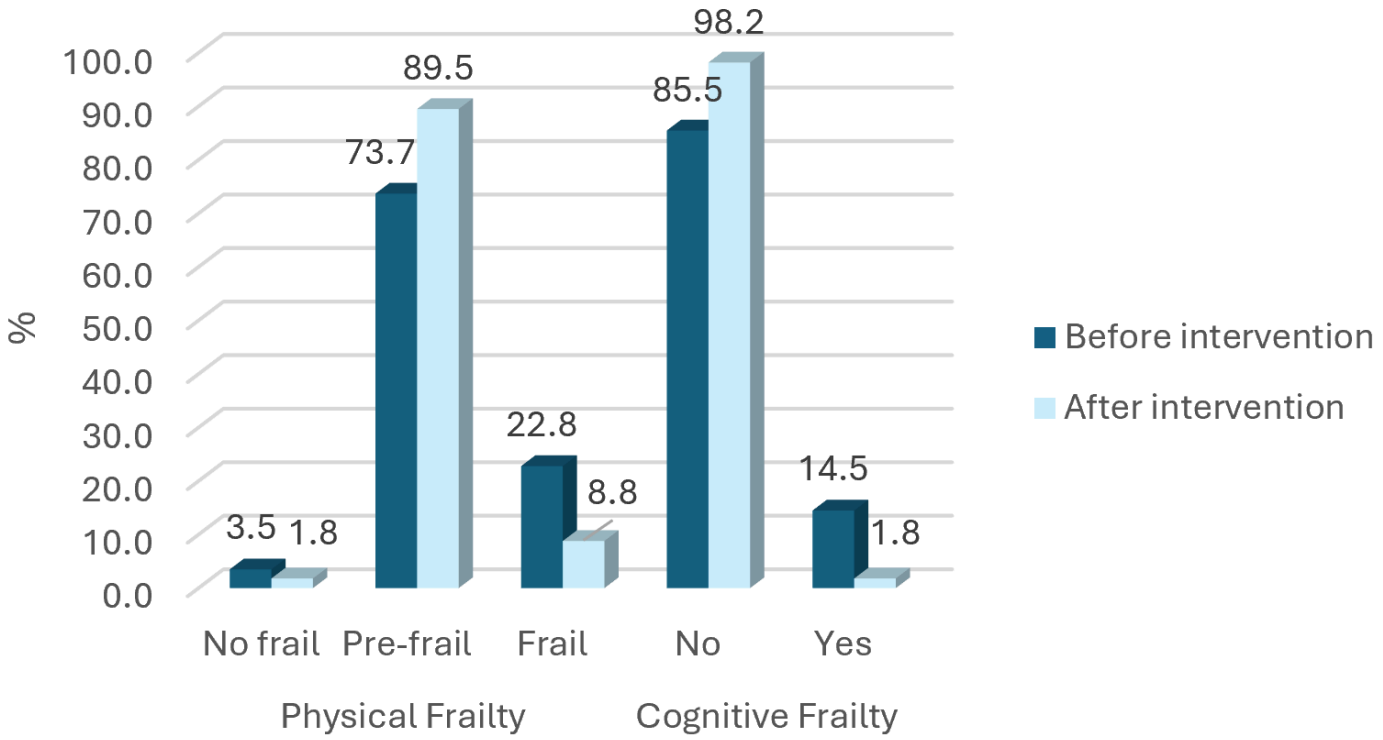


Figure 1

Physical and Cognitive Frailty Assessment

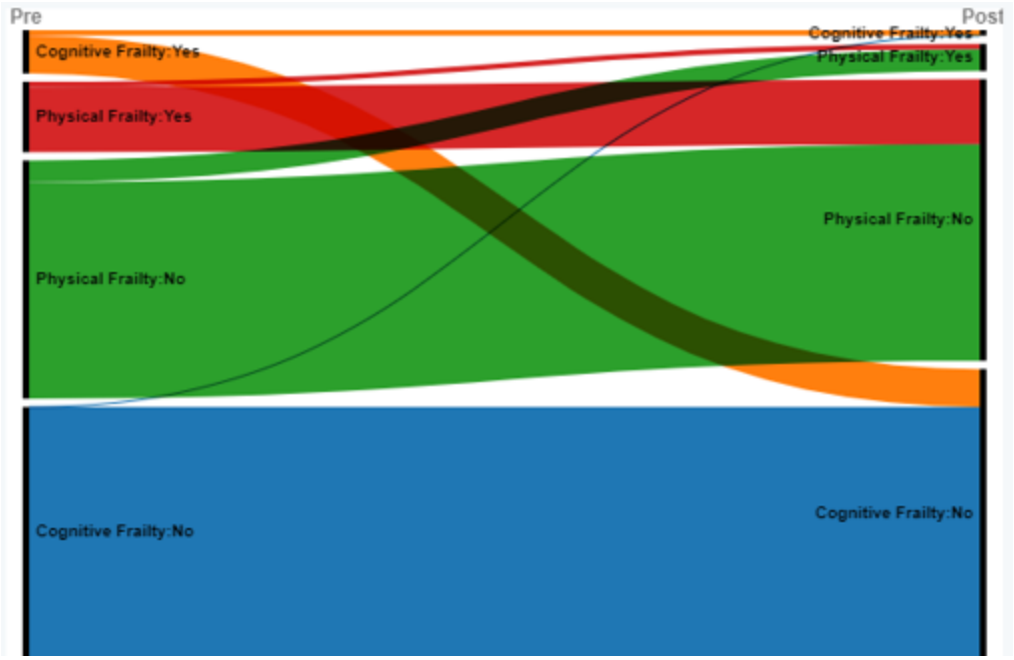


Figure 2

Sankey diagram showing transitions in cognitive and physical frailty status from pre- to post-intervention. Flow width represents the number of participants, highlighting shifts toward less frail states.