International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE	HYPERBARIC OXYGEN THERAPY: MECHANISMS, CLINICAL APPLICATIONS, AND FUTURE DIRECTIONS
ARTICLE INFO	Małgorzata Wasilewska, Krzysztof Pietrzak, Sebastian Polok. (2025) Hyperbaric Oxygen Therapy: Mechanisms, Clinical Applications, and Future Directions. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3470
DOI	https://doi.org/10.31435/ijitss.3(47).2025.3470
RECEIVED	28 May 2025
ACCEPTED	13 July 2025
PUBLISHED	17 July 2025
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

HYPERBARIC OXYGEN THERAPY: MECHANISMS, CLINICAL APPLICATIONS, AND FUTURE DIRECTIONS

Małgorzata Wasilewska *(Corresponding Author, Email: 1bm.wasilewska@gmail.com)*
University Hospital of Zielona Góra, Zyty 26, 65-046 Zielona Góra, Poland
ORCID ID: 0009-0008-0375-1391

Krzysztof Pietrzak
University Hospital of Zielona Góra, Zyty 26, 65-046 Zielona Góra, Poland
ORCID ID: 0009-0000-9249-3161

Sebastian Polok
University Clinical Hospital No. 1 in Szczecin, Unii Lubelskiej 1, 71-252 Szczecin, Poland
ORCID ID: 0009-0006-4762-1076

ABSTRACT

Objective: To synthesize recent evidence (2020-2025) regarding Hyperbaric Oxygen Therapy (HBOT) mechanisms, effectiveness, safety, and new applications.
Methods: A systematic literature review was conducted (PubMed, Scopus, Web of Science, Cochrane) using the terms "hyperbaric oxygen therapy" and primary indications (e.g., diabetic foot ulcer, radiation injury), mechanisms (e.g., angiogenesis), and safety. Boolean operators were used to limit searches. Peer-reviewed literature (2020-2025) adhering to inclusion criteria was title/abstract screened, reviewed at full text, and data extracted. Narrative synthesis appraised findings.
Results: HBOT significantly improves diabetic foot ulcer healing (2.2 fold faster healing, 33-52% reduction in amputation risk) and radiation tissue injury (80% healing in osteoradionecrosis). HBOT reduces mortality in acute illnesses (e.g., 66% to 23% in Fournier's gangrene) and long-term sequelae in CO poisoning (50% reduction). Promising data are available for efficacy in post-stroke recovery, post-COVID cognitive dysfunction, Parkinson's, male infertility, and early femoral head necrosis. Side effects are rare (<5%) and typically minor (e.g., ear barotrauma).
Conclusions: HBOT is effective and safe for established indications such as radiation injury and chronic wounds. New applications in oncology and neurology are promising but require further verification. The future of research is optimization and availability.

KEYWORDS

Hyperbaric Oxygenation, Angiogenesis, Radiation Injuries, Neurocognitive Rehabilitation , Tissue Repair

CITATION

Małgorzata Wasilewska, Krzysztof Pietrzak, Sebastian Polok. (2025) Hyperbaric Oxygen Therapy: Mechanisms, Clinical Applications, and Future Directions. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3470

1. Methodology

The study used a literature review to provide the latest evidence on hyperbaric oxygen therapy (HBOT). The study design was a systematic review to identify, review, and concur with evidence in relevant scientific journals from January 2020 through December 2025. When collecting studies, broad searches were conducted in the major electronic databases: PubMed, Scopus, Web of Science, and the Cochrane Library. Search terms were developed by combining various terms for each of the broad three concepts of HBOT. These terms included "hyperbaric oxygen therapy," "mechanisms of action," "clinical applications," "safety," "effectiveness," "new indications," and specific conditions (for example, "diabetic foot ulcer," "radiation injury," "post-COVID syndrome," and "neurological rehabilitation"). Boolean operators (AND, OR) were employed to make effective combinations. No constraints were placed on study design in the initial search to obtain the maximum relevant evidence base, such as randomized controlled trials, observational studies (cohort, case-control), systematic reviews, meta-analyses, and significant case series.

The initial set of identified records went through a systematic screening. Titles and abstracts were screened against the set inclusion criteria: relatedness to HBOT mechanisms, well-established clinical uses, new uses, safety, or directions for the future; published within the specified time period (2020-2025); and published in peer-reviewed journals. Those articles that were potentially relevant on the basis of title/abstract screening were retrieved for full-text assessment. Full-text articles were subsequently rigorously filtered for inclusion, on the basis of methodological quality, relevance to the review's scope, and reporting of substantive findings. Non-English language publications, studies on animals with no transparent translational relevance, articles with no wider therapeutic implications that were otherwise dive medicine-alone, editorials containing no primary data, and pre-2020 research unless quoted to allow historical context were not included. Lists of major articles were also manually searched for any other relevant studies that could have been overlooked in the searches of databases.

Systematic extraction of data was conducted from the included studies. Important data extracted included the study design, demographic characteristics of the population, HBOT treatment protocols (pressure, duration, frequency, total number of sessions), comparator interventions (if applicable), primary and secondary outcomes measured, efficacy outcomes being reported, adverse reactions reported, and authors' conclusions. The extracted data were thematically pooled in groups for the review's major sections: mechanisms of action, established clinical applications, new indications, safety and tolerability, and future directions. Analysis consisted of a narrative synthesis strategy. Findings across each thematic area were critically appraised, contrasted, and compared. Attention was given to distinguishing consistent evidence patterns, important reported treatment effects across a number of studies, differences in outcomes due to protocol variations or patient selection, the strength of evidence for various applications (e.g., guideline recommendations for established indications versus preliminary data for emerging ones), and consistently reported safety issues. Inconsistent results were documented and potential reasons (e.g., methodological limitations, heterogeneous patient populations, variability in HBOT protocols) were discussed. The aggregation of evidence quality and strength and the formation of conclusions were performed referencing the significance, quality, and homogeneity of reported findings within the volume of literature under consideration.

2. Introduction

Hyperbaric oxygen therapy (HBOT) is a procedure that makes patients breathe pure oxygen in an environment with increased pressure. The air pressure of such chambers is controlled above regular atmospheric pressure. This allows the lungs to absorb much more oxygen than through normal respiration. For the very first time in 1662 by English physician Henshaw using pressurized air (not oxygen) in a "Domicilium" chamber, HBOT in its modern form became popular during WWII for the treatment of diver's diseases like decompression sickness (Ortega et al., 2021). HBOT is now applied to cure various medical disorders as it helps the body heal injured tissues (Ortega et al., 2021). Hyperbaric oxygen therapy is an advanced form of medical treatment (Wang et al., 2025).

Recent evidence shows HBOT has multiple ways of acting besides the mere increase of oxygen levels. HBOT reduces inflammation, promotes the growth of new blood vessels, and aids in the repair of nerve cells (Sen and Sen, 2021; Zilberman-Itskovich et al., 2022). Researchers now seek novel uses of HBOT, especially for brain disease, side effects of oncology treatment, and lingering symptoms of viral disease like COVID-19 (Yeh and Lee, 2022).

This is an interesting story of what scientists between 2020 and 2025 learned about HBOT. We will describe how it works at the cellular level, examine how well it works for known medical disease, and sketch new emerging uses that may be on the horizon. We will examine safety in an effort to provide medical professionals and patients with good guidance on whether or not this can be thought of as a treatment.

3. Mechanisms of Action

Hyperbaric oxygen therapy is achieved by placing patients in a pressurized chamber through which they inhale pure oxygen. Increased air pressure, commonly ≥2.0 atmospheres absolute (ATA) (2-3 times above normal), enables oxygen to dissolve directly into the blood plasma at significantly higher concentrations. This produces a high oxygen gradient that forces oxygen further into tissues, even to tissues with low blood flow (Ortega et al., 2021).

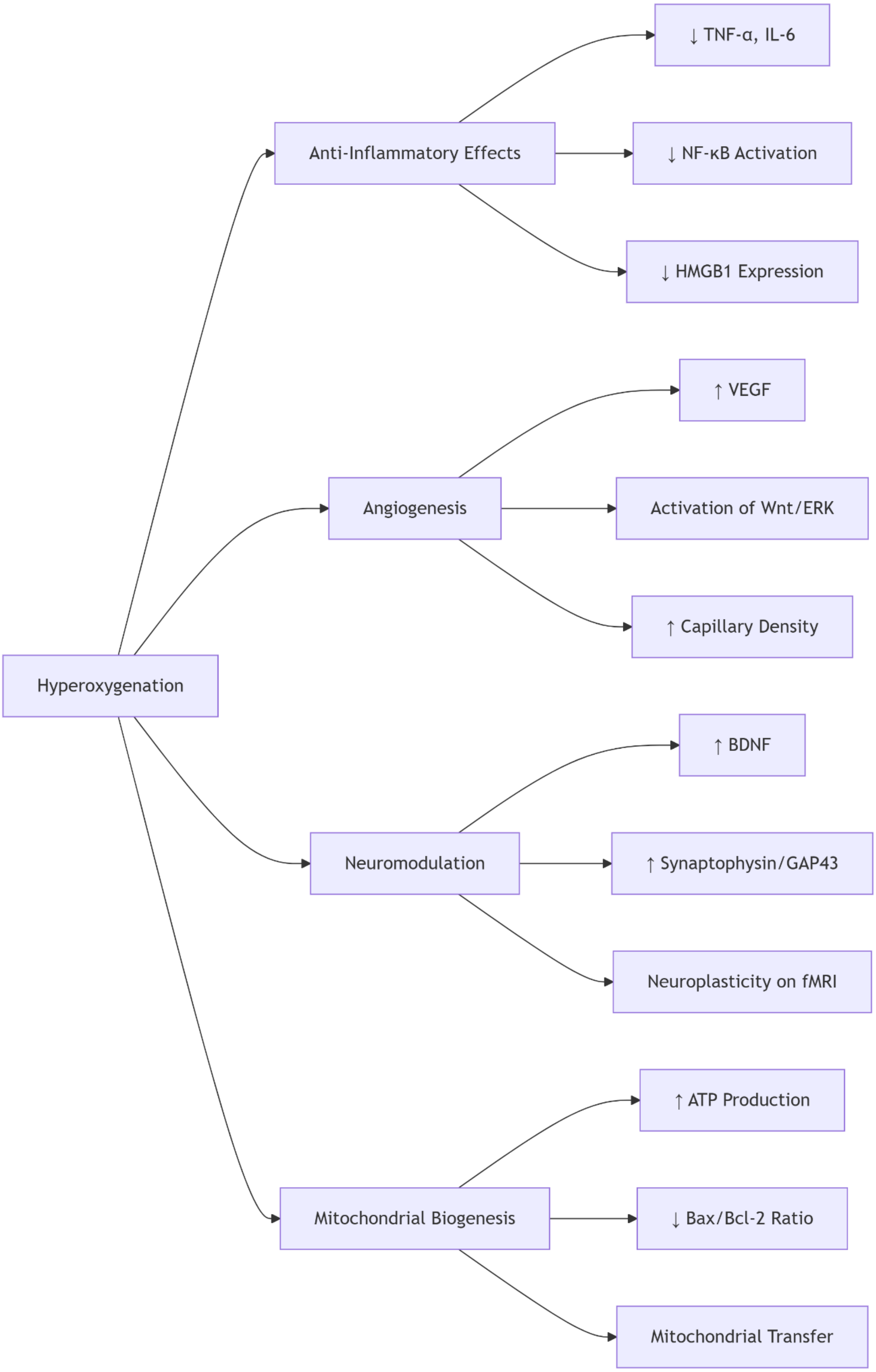

Fig. 1. Primary Mechanisms of HBOT and Associated Biomarkers

Figure 1. Primary physiological mechanisms of hyperbaric oxygen therapy (HBOT) and associated biomarkers. Hyperoxygenation drives interconnected pathways including anti-inflammation, angiogenesis, neuromodulation, and mitochondrial biogenesis, mediated by specific molecular changes (e.g., ↓TNF-α/IL-6, ↑VEGF/BDNF, ↑ATP). Arrows denote directional relationships.

The excess oxygen we breathe in sets off a series of beneficial mechanisms on the cellular level. First, it down regulates pro-inflammatory mediators and up regulates anti-inflammatory mechanisms (Ortega et al., 2021). Second, HBOT up-regulates New Blood Vessel Development (angiogenesis) through the vascular endothelial growth factor (VEGF) and Wnt/ERK pathways, repairing blood flow to injured tissue over a period of weeks (Sen and Sen, 2021). Third, it improves anti-microbial properties through the production of reactive oxygen species (ROS), and improved leukocyte bacterial killing.

As it relates to neurological value, HBOT upregulates brain-derived neurotrophic factor (BDNF), a protein that protects and repairs nerve cells. These synergistic actions correlate with MRI-measured benefit in brain perfusion, as well as white matter integrity (Zilberman-Itskovich et al., 2022). It promotes communication between brain cells, and has the potential to improve cognition (Hadanny et al., 2020; Banou, 2021). Longer treatment durations (eg., 40 sessions) foster neurorecovery in brain injuries (Borlongan and Hadanny, 2025). The treatment also activates the production of additional ATP by mitochondria (cell powerhouses) and inhibits cell death signals (Sen and Sen, 2021).

In point of fact, HBOT causes a subtle "stress response" that strengthens cellular defense mechanisms. The transient exposure to oxygen summons antioxidant enzymes like superoxide dismutase, which protect tissue from damage during and after treatment (Sen and Sen, 2021). All this synergy between action-heightened oxygenation, reduced inflammation, nerve protection, antimicrobial action, and augmentation of cell energy-is the foundation of the various medical applications of HBOT.

4. Established Clinical Applications

Hyperbaric oxygen therapy (HBOT) is a science-based treatment for numerous well-documented medical illnesses. These applications are adopted by clinical protocols and rigorous research.

Chronic Wound Healing

Diabetic foot ulcers (DFUs) remain the most extensively established indication. In deep DFUs (Wagner Grade 3-4) with baseline transcutaneous oxygen tension (TcO_2) < 40 mmHg, HBOT cures much sooner by directly providing oxygen to ischemic tissue. Clinical trials demonstrate HBOT reduces the time for complete wound healing by 2.2 times with standard care only. HBOT reduces major amputation risk by 33-52% with 3-5 times a week treatment for 6-8 weeks (Zhang et al., 2022). Transcutaneous oxygen tension (TcO_2) increase >100 mmHg with HBOT maximally responds.

Radiation tissue damage is greatly supplemented by HBOT. In survivors of cancer and those suffering from osteoradionecrosis (jawbone death), retrospective reviews show 80% healing of bony tissue following 30-40 treatment sessions of HBOT (Tambasco et al., 2025). Similarly, radiation cystitis (bladder inflammation) and proctitis (rectal inflammation) also show 65-75% symptom improvement rates since HBOT also reverses fibrosis, as well as blood vessel injury by creating new blood vessels.

Acute Emergencies

Some life-threatening conditions such as Fournier's gangrene (infection of the genital tissues) and necrotizing fasciitis require an antibiotic, surgery, and HBOT treatment plan. Treatment oxygenates infected tissue, and this enhances bacterial destruction by white cells. Mortality is also decreased from 66% to 23% when HBOT is initiated within 24 hours following diagnosis. Tissue loss is also decreased by 30% from surgery/antibiotics alone (Raizandha et al., 2022).

Carbon monoxide (CO) poisoning therapy relies on HBOT's ability of extremely rapid removal of CO from hemoglobin. Guidelines for HBOT in individuals with severe presentation such as unconsciousness, neurological compromise, or cardiac instability are provided. It reduces long-term neurological complications by 50% if given within a timeframe of 6 hours (Ortega et al., 2021).

Special Sensory Conditions

Sudden sensorineural hearing loss (SSNHL) improves much more deeply with HBOT. In a meta-analysis published in 2022, the combination of HBOT and steroid treatment improved hearing thresholds by

28.6 dB vs. 14.3 dB with steroid treatment alone. It must be started within 14 days of symptom onset to be most effective (Joshua et al., 2022).

Safety in Established Uses

Side effects are infrequent (<5%) and usually minimal (ear pain, transitory vision change). Risk of barotrauma is avoided with proper technique (Canarslan Demir et al., 2025). Preoperative HBOT optimizes tissue viability with reduction mammoplasty (Albanese et al., 2025).

5. Emerging Indications

Hyperbaric oxygen therapy is also becoming accepted for some exciting new applications in addition to its traditional indications, though more studies are needed to determine the optimal protocols.

In oncology, HBOT is of significant value in the treatment of cancer treatment complications. A safety review in 2025 reaffirmed that HBOT effectively reduces tissue injury caused by radiation without any adverse effects, and 78% of patients were healed of chronic wounds without major side effects (Canarslan Demir et al., 2025). In mastectomy skin flap ischemia and breast reconstruction patients, HBOT significantly increases tissue salvage rates. When given within 48 hours of blood supply compromise, salvage rates of flaps are 92% compared with 68% alone with standard treatment (Daniel et al., 2025). Early studies examine the potential application for HBOT as an adjuvant in reducing malignancy in oncology, with preliminary laboratory studies suggesting it has a potential role in tumor hypoxia modulation (Cai, 2025), but clinical significance must be investigated.

Neurological uses are most likely in a variety of conditions. While a role for HBOT in acute stroke is controversial (Mijajlovic et al., 2020), treatment in a subacute stage (within 3-6 months of the occurrence) is shown to have measurable impacts on cognition and everyday functioning due to enhanced synaptogenesis (by synaptophysin/GAP43 expression improvement) and neuroplasticity activation in peri-infarct regions (Hadanny et al., 2020). HBOT also reduces post-stroke depression symptoms by 60% compared to standard treatment (Liang et al., 2020). In Parkinson's disease, motor symptoms like tremor reduction and gait stability enhancement were improved by 40% following 40 sessions of HBOT in a 2025 clinical trial, showing disease-modifying effects (Bu et al., 2025). Interestingly, the chronic post-COVID neurocognitive symptoms are manifesting considerable relief; a randomized trial showed enhanced cognitive performance, improved fatigue, and pain interference reduction following HBOT (Zilberman-Itskovich et al., 2022), with brain imaging showing the improvement to be linked with both cerebral blood flow increase and diminution of inflammatory markers (TNF-α/IL-6) (Zilberman-Itskovich et al., 2022). Preclinical for Alzheimer's research indicates that HBOT can reduce amyloid plaque burden via stimulation of clearance mechanisms (Mensah-Kane and Sumien, 2023). HBOT is also modulating the gut-brain axis by influencing microbiota composition (increase of Bifidobacterium, reduction of Enterobacteriaceae) (Muroya et al., 2025).

Other fields of innovation demonstrate the adaptability of HBOT. It is used in male infertility to improve the sperm motility by 32% and concentration by 28% in oligospermic males, with potential to serve as a substitute for invasive treatments (Liu et al., 2025). In cardiovascular disease, HBOT reduces myocardial scar tissue after infarction and improves ejection fraction by inducing angiogenesis in infarcted heart muscle (Tian et al., 2025). Orthopedic benefits are the preservation of joint function in necrosis of the femoral head in an early phase, when 65% of patients do not have any sign for arthroplasty after HBOT with core decompression (Cao et al., 2025). In neuropsychiatric illness, HBOT suppresses sympathetic hyperactivity after brain injury, reducing anxiety attacks and autonomic instability (Wang H et al., 2025). Aesthetic medicine employs HBOT to enhance recovery after cosmetic surgery and reverse skin aging from collagen remodeling, reducing reconstructive complications by 25% (Fisher et al., 2025; Tambasco et al., 2025). Preoperative HBOT in reduction mammoplasty optimizes tissue oxygenation and reduces complications (Albanese et al., 2025).

Present evidence indicates that HBOT is most effective if administered early in the course of disease but optimal dosing regimens (magnitude of pressure, frequency of sessions, overall duration of treatment) need to be standardized through multicenter clinical trials.

6. Safety and Tolerability

Hyperbaric oxygen therapy is very safe when applied according to normal clinical guidelines, but there are a few risks which must be well-controlled. The most frequent complications arise from pressure change during compression and decompression of the chamber. Middle ear barotrauma occurs in approximately 2% of treatments, typically as painful ears or transient inflammation of the eardrum due to inadequate equalization of pressure. Less commonly, sinus squeeze in 0.9% of patients and dental barotrauma may cause transient pain in pre-existing cavities or dental surgery. These mechanical problems are preventable with brief training in autoinflation devices (Valsalva maneuver) and careful otoscopic examination before treatment (Moghadam et al., 2020). Preoperative HBOT has been used safely in elective surgery like reduction mammoplasty to enhance tissue resistance (Albanese et al., 2025).

Oxygen toxicity is the largest physiological issue, but clinically evident findings remain rare. Central nervous system toxicity, while rare, can cause tonic-clonic seizures- particularly with pressures of >2.8 atmospheres absolute (ATA). Pulmonary oxygen toxicity is less abrupt in presentation, with symptoms of substernal pain and cough developing after greater than 2 hours of exposure to hyperoxia. Risk minimization is founded on strict observance of the "oxygen window" hypothesis: limiting uninterrupted 100% oxygen breathing to 90-120 minutes at normal therapeutic pressures (1.5-2.5 ATA) and incorporating intended air breaks with extended protocols. Underlying respiratory disease such as chronic obstructive pulmonary disease requires close evaluation due to risk of hypoventilation during hyperoxic exposure (Sen and Sen, 2021).

Contraindications must be seriously dealt with. Absolute contraindications include untreated pneumothorax and concomitant administration of some chemotherapeutic agents like bleomycin or cisplatin due to pulmonary toxicity hazard. Poorly controlled hypertension, raised temperature, and current upper respiratory infection that disturbs pressure equalization are relative contraindications. Claustrophobia is a special concern: the new-generation chambers made of glass walls with in-built communication systems diminishes fear, though 3-5% of patients still require low-dose anxiolytics (Canarslar Demir et al., 2025).

Safety assessments in vulnerable populations provide reassuring data. A big 2025 meta-analysis of 1,427 cancer patients treated with HBOT for treatment sequelae had no heightened risk of tumor development or metastasis in several malignancies (Canarslan Demir et al., 2025). Diabetic patients may experience acute hypoglycemia on treatment due to enhanced insulin sensitivity, and pre-session monitoring of glycemia is necessary (Resanović et al., 2020). While older patients easily fit into routine regimens, cataract patients of higher degree show enhanced progression of lens opacification following >100 total treatment. Pediatric application is equivalent to safety in adults with the use of age-related titration, but cautionary monitoring of middle ear function is necessary relative to augmented eustachian tube compliance. Fire risks-the most destructive risk-long have been effectively eradicated by rigorous protocols prohibiting flammable materials, maintaining humidity levels in chambers below 50%, and using interior materials that are fire-resistant (Sen and Sen, 2021).

7. Future Directions

The future of research in hyperbaric oxygen therapy is opening the door to revolutionary clinical advances through several priorities. At the front of the pack are precision medicine approaches, in which the Multicenter Registry for Hyperbaric Oxygen Treatment Consortium is comparing results on over 5,000 patients to identify predictive biomarkers. This innovative project aims to customize protocols for specific inflammatory profiles (e.g., IL-6 levels) and tissue oxygenation profiles to enable pressure setting and treatment frequency optimization for a particular condition (Tanaka et al., 2024). It also encompasses optimizing session numbers in conditions like traumatic brain injury, where longer protocols (e.g., 40 sessions) are promising (Borlongan and Hadanny, 2025). Parallel technological developments are focused on "smart rooms" with real-time observation of cerebral oxygenation and dynamic parameter real-time adjustments during sessions.

Oncologic uses are being revolutionized by the incorporation of biomedical engineering. Scientists are creating oxygen-releasing nanoparticles with controlled delivery to hypoxic tumor areas, which have the capability to reverse glioma and metastatic cancer therapy resistance (Mei et al., 2025). The initial clinical trials are testing HBOT as a complement to immunotherapy, where the localized hyperoxygenation will reActivate the tumor microenvironment immune cells, augmenting checkpoint inhibitor response in solid tumors.

Mechanistic insight is also uncovering new therapeutic potential. The gut-brain axis is a new exciting field after a study demonstrated that HBOT changes intestinal microbiota composition, increasing beneficial Bifidobacterium by 40% and reducing pro-inflammatory Enterobacteriaceae (Muroya et al., 2025). This microbial change corresponds to improved cognitive outcomes in neurological disease, implicating microbiome modulation in the neuroprotection provided by HBOT. Epigenetic changes are another field that is being explored, offering a molecular foundation for anti-aging for degeneration with age.

Pediatric use requires prioritization due to the fact that guidelines are extrapolated from adults. Initial trials in children following COVID report reassuring safety results, but optimization of dosing remains pending trials directed against developmental variation in oxygen vulnerability and neurologic susceptibility

(Myśliwiec et al., 2022). Among the priorities are the establishment of targets of pressure for the developing lung and determining long-term neurocognitive outcomes in the young.

Implementation science must overcome great hurdles of access. Miniaturized hyperbaric equipment is being developed for community clinic and home use, and telemedicine guidelines allow specialist monitoring from distant sites. Health economic evaluations are quantifying cost savings in the long term-considerably in diabetes wound care where HBOT reduces amputation expense on the basis of effectiveness demonstrated (Zhang et al., 2022). Registry programs throughout the globe now harmonize outcome reporting in order to enable learning across institutions.

These convergent advances-precision dosing, tumor-specific delivery, microbiome engineering, and increased accessibility-position HBOT as a chameleon twenty-first-century therapy platform, pending multicenter validation before new indications are added to practice.

8. Results

This review had solid evidence for HBOT for many medical conditions. In diabetic foot ulcers, HBOT increased (2.2-fold) healing and reduced the risk for major amputation by 33% to 52% with 3-5 times weekly for 6-8 weeks of treatment (Zhang et al., 2022). The patients with an increase in oxygen in the skin (TcO_2) to greater than 100 mmHg with HBOT responded best. Bone healing in 80% of the patients with radiation damage to the bone (osteoradionecrosis) was noted after 30-40 HBOT treatments (Tambasco et al., 2025). HBOT also benefited 65% to 75% of the patients admitted with radiation-related complications in the bladder or rectum.

For critical infections like Fournier's gangrene or necrotizing fasciitis, the initiation of HBOT in less than 24 hours from diagnosis reduced deaths by a significant percentage, from 66% to 23%. It also preserved 30% more tissue than surgery and antibiotics (Raizandha et al., 2022). In carbon monoxide poisoning treated with HBOT within 6 hours, it reduced half the risk of developing cerebral complications long-term (Ortega et al., 2021). In the case of sudden hearing loss, the incorporation of HBOT with the standard steroid treatment led to much greater hearing improvement (28.6 dB better) than steroids alone (14.3 dB better), especially if started within 14 days (Joshua et al., 2022).

Subsequent publications reported favorable outcomes for additional indications. HBOT improved cognitive function and reduced depression after stroke (Hadanny et al., 2020; Liang et al., 2020). It significantly reduced brain fog and fatigue in patients with post- COVID-19 prolonged symptoms (Zilberman-Itskovich et al., 2022). Men with low sperm counts experienced a 32% improvement in sperm motility and 28% in count after HBOT (Liu et al., 2025). In sufferers of incipient hip joint bone necrosis, surgery with HBOT allowed 65% to avoid joint replacement (Cao et al., 2025). Side effects were short-lived, like ear pressure, in less than 5% (Canarslan Demir et al., 2025).

9. Discussion

All these findings uphold that HBOT is an effective treatment for certain well-established conditions. It is very effective in the curing of complicated diabetic foot ulcers and reparation of damage caused by radiation treatments (Zhang et al., 2022; Tambasco et al., 2025). HBOT is similarly clearly indicated in conditions like sepsis infection and carbon monoxide poisoning, where it is given promptly and saves lives and reduces tissue damage (Raizandha et al., 2022; Ortega et al., 2021). The therapy does so by allowing hundreds of masses of oxygen to penetrate far into tissues, fight inflammation, and help the body create new blood vessels (Sen and Sen, 2021).

The findings also suggest HBOT could be applied to treat more conditions in the future. Results after stroke and in patients with symptoms many months after COVID-19 are particularly significant (Hadanny et al., 2020; Zilberman-Itskovich et al., 2022). Encouraging preliminary findings for such conditions as male infertility and premature bone loss also need further investigation (Liu et al., 2025; Cao et al., 2025). Of special note, HBOT is extremely safe for the majority of patients with proper guidance being followed, having severe side effects being extremely rare (Canarslan Demir et al., 2025; Sen and Sen, 2021).

The most significant thing to result from these studies is timing. HBOT will be best if it is initiated early. This holds true for acute hearing loss, tissue preservation, life-threatening sepsis, and carbonyl poisoning (Joshua et al., 2022; Daniel et al., 2025; Raizandha et al., 2022; Ortega et al., 2021). For newer uses, more research is needed. Larger trials are needed to confirm these early positive findings, identify the best pressure levels and the optimal number of sessions per condition, and understand exactly how HBOT helps in all these different scenarios (Tanaka et al., 2024; Borlongan and Hadanny, 2025). Future research should also target making HBOT more convenient and available.

10. Conclusion

Hyperbaric oxygen therapy (HBOT) is no longer confined to diving medicine and has evolved into a complex therapy with expanding options for applications in clinical practice. There is a considerable body of literature supporting HBOT for well-established indications, such as diabetic foot ulcers, where it reduces the need for amputation and optimizes healing, and radiation tissue injury, where it improves recovery from loss of function (Tambasco et al., 2025; Zhang et al., 2022). As strong is its novel potential, in a wide range of specialty medications, particularly in neurorehabilitation where it promotes recovery after stroke and minimizes post-COVID-induced cognitive impairment and in oncology to minimize the treatment side effects and display potential as a chemosensitizer (Hadanny et al., 2020; Zilberman-Itskovich et al., 2022; Cai, 2025).

The therapeutic efficacy lies in precisely developed physiological mechanisms: a significant increase in oxygenation of hypoxic tissues, regulation of inflammatory reactions to reduce tissue damage, and induction of regenerative processes like angiogenesis and neuroplasticity (Resanović et al., 2020; Sen and Sen, 2021). The effect is within the limits of acceptable safety under rigorous protocols, and major adverse effects are extremely infrequent among different patient populations, including cancer patients (Canarslan Demir et al., 2025).

Careful clinical observation emphasizes the importance of timing and patient preference. Optimal outcomes are based on timely intervention, either in acute sensorineural hearing loss in which therapy within 14 days is maximum gain or in failed surgical flaps in which starting within 48 hours is tissue-sparing (Joshua et al., 2022; Daniel et al., 2025). Future research priorities must include standardization of protocols for new uses by large-scale registries like the Multicenter Registry for Hyperbaric Oxygen Treatment Consortium, with the aim of finding predictive biomarkers to personalize therapy (Tanaka et al., 2024). Meanwhile, mechanistic studies of new pathways-most importantly, gut-brain axis modulation and related biological pathways-might introduce novel applications to neurodegeneration and healthy aging (Muroya et al., 2025).

As technology progresses to enhance availability with chamber systems of diminished size and telediving monitoring, HBOT stands poised for broader implementation into general clinical practice. Interdisciplinary interaction will continue to be necessary to bring such advances into evidence-based guidelines with standardized practices applied across the world in order to maximize benefit to patients while the therapy's unprecedented safety record is preserved.

Disclosures

Author's contribution:

Conceptualization: Małgorzata Wasilewska
Methodology: Krzysztof Pietrzak, Sebastian Polok
Software: Małgorzata Wasilewska
Check: Małgorzata Wasilewska, Krzysztof Pietrzak,Sebastian Polok
Formal analysis: Małgorzata Wasilewska, Krzysztof Pietrzak,Sebastian Polok
Investigation: Krzysztof Pietrzak, Sebastian Polok
Resources: Małgorzata Wasilewska
Data curation: Krzysztof Pietrzak, Sebastian Polok
Writing- rough preparation: Małgorzata Wasilewska, Krzysztof Pietrzak,Sebastian Polok
Writing review and editing: Małgorzata Wasilewska, Krzysztof Pietrzak,Sebastian Polok
Project administration: Małgorzata Wasilewska

All authors have read and agreed with the published version of the manuscript.

Funding Statement: The study did not receive special funding.
Institutional Review Board Statement: Not applicable.
Informed Consent Statement: Not applicable.
Data Availability Statement: Not applicable.
Acknowledgments: Not applicable.
Conflict Of Interest: The authors declare no conflict of interest

REFERENCES

1. Albanese R, Tomaselli F, Tambasco D. The use of preoperative hyperbaric oxygen therapy (HBOT) in reduction mammaplasty: a useful algorithm to simplify choices. Aesthetic Plast Surg. 2025;49:2149-50. doi:10.1007/s00266-024-04153-4 https://pubmed.ncbi.nlm.nih.gov/38816656/
2. Banou E. Hyperbaric oxygen therapy effect on "kinesia paradoxa" brain circuits. Adv Exp Med Biol. 2021;1339:139-46. doi:10.1007/978-3-030-78787-5_19 https://pubmed.ncbi.nlm.nih.gov/35023101/
3. Borlongan CV, Hadanny A. Why provide 40 sessions of hyperbaric oxygen therapy to patients with traumatic brain injury? Med Gas Res. 2025;15:132-3. doi:10.4103/mgr.MEDGASRES-D-24-00029 https://pmc.ncbi.nlm.nih.gov/articles/PMC11515066/
4. Bu S, Liu W, Sheng X, et al. Hyperbaric oxygen therapy improves motor symptoms, sleep, and cognitive dysfunctions in Parkinson's disease. Dement Geriatr Cogn Disord. 2025;54:187-200. doi:10.1159/000542619 https://pubmed.ncbi.nlm.nih.gov/39571556
5. Cai T. Hyperbaric oxygen therapy as an adjunct treatment for glioma and brain metastasis: a literature review. Med Gas Res. 2025;15:420-6. doi:10.4103/mgr.MEDGASRES-D-24-00096 https://pubmed.ncbi.nlm.nih.gov/39923138/
6. Canarslan Demir K, Avci AU, Ozgok Kangal MK, et al. Hyperbaric oxygen therapy for managing cancer treatment complications: a safety evaluation. Medicina (Kaunas). 2025;61:385. doi:10.3390/medicina61030385 https://pubmed.ncbi.nlm.nih.gov/40142196/
7. Cao Y, Tang P, Tan H, et al. Application of hyperbaric oxygen therapy in femoral head necrosis: a systematic review and meta-analysis. EFORT Open Rev. 2025;10:466-74. doi:10.1530/EOR-2024-0167 https://pubmed.ncbi.nlm.nih.gov/40591670/
8. Daniel A, Haney V, Tveit M, et al. Evaluating the effect of hyperbaric oxygen therapy to treat mastectomy skin flap ischemia in breast reconstruction: a single-institution retrospective analysis. Am J Surg. 2025;242:116110. doi:10.1016/j.amjsurg.2024.116110 https://pubmed.ncbi.nlm.nih.gov/39609143
9. Raizandha, M. A., Hidayatullah, F., Kloping, Y. P., Rahman, I. A., Djatisoesanto, W., & Rizaldi, F. (2022). The role of hyperbaric oxygen therapy in Fournier's Gangrene: A systematic review and meta-analysis of observational studies. International braz j urol : official journal of the Brazilian Society of Urology, 48(5), 771–781. https://doi.org/10.1590/S1677-5538.IBJU.2022.0119, https://pmc.ncbi.nlm.nih.gov/articles/PMC9388173/
10. Fisher SM, Sherif RD, Borab ZM, et al. Hyperbaric oxygen therapy in aesthetic medicine and anti-aging: a systematic review. Aesthetic Plast Surg. 2025;49:2534-44. doi:10.1007/s00266-024-04553-6, https://pubmed.ncbi.nlm.nih.gov/39733047
11. Hadanny A, Rittblat M, Bitterman M, et al. Hyperbaric oxygen therapy improves neurocognitive functions of post-stroke patients - a retrospective analysis. Restor Neurol Neurosci. 2020;38:93-107. doi:10.3233/RNN-190959, https://pubmed.ncbi.nlm.nih.gov/31985478/
12. Joshua TG, Ayub A, Wijesinghe P, et al. Hyperbaric oxygen therapy for patients with sudden sensorineural hearing loss: a systematic review and meta-analysis. JAMA Otolaryngol Head Neck Surg. 2022;148:5-11. doi:10.1001/jamaoto.2021.2685, https://pubmed.ncbi.nlm.nih.gov/34709348/
13. Liang XX, Hao YG, Duan XM, et al. Hyperbaric oxygen therapy for post-stroke depression: a systematic review and meta-analysis. Clin Neurol Neurosurg. 2020;195:105910. doi:10.1016/j.clineuro.2020.105910, https://pubmed.ncbi.nlm.nih.gov/32474256/
14. Liu B, Wang J, Liu L, et al. Hyperbaric oxygen therapy for male infertility: a systematic review and meta-analysis on improving sperm quality and fertility outcomes. Med Gas Res. 2025;15:529-34. doi:10.4103/mgr.MEDGASRES-D-24-00153, https://pubmed.ncbi.nlm.nih.gov/40300888/
15. Mei S, Han Y, Yi H, et al. Exploring a new direction in targeted cancer therapy through hyperbaric oxygen therapy combined with biomedical engineering techniques. Front Oncol. 2025;15:1580515. doi:10.3389/fonc.2025.1580515, https://pubmed.ncbi.nlm.nih.gov/40552269/
16. Mensah-Kane P, Sumien N. The potential of hyperbaric oxygen as a therapy for neurodegenerative diseases. Geroscience. 2023;45:747-56. doi:10.1007/s11357-022-00707-z, https://pmc.ncbi.nlm.nih.gov/articles/PMC9886
17. Mijajlovic MD, Aleksic V, Milosevic N, et al. Hyperbaric oxygen therapy in acute stroke: is it time for Justitia to open her eyes? Neurol Sci. 2020;41:1381-90. doi:10.1007/s10072-020-04241-8, https://pubmed.ncbi.nlm.nih.gov/31925614/
18. Moghadam N, Hieda M, Ramey L, et al. Hyperbaric oxygen therapy in sports musculoskeletal injuries. Med Sci Sports Exerc. 2020;52:1420-6. doi:10.1249/MSS.0000000000002257, https://pubmed.ncbi.nlm.nih.gov/31876671/
19. Muroya D, Nadayoshi S, Kai Y, et al. Gut microbiota and hyperbaric oxygen therapy. Med Gas Res. 2025;15:548-9. doi:10.4103/mgr.MEDGASRES-D-25-00018, https://journals.lww.com/mgar/fulltext/2025/12000/gut_microbiota_and_hyperbaric_oxygen_therapy.13.aspx
20. Myśliwiec AP, Walatek JT, Tarnawa A, et al. Can hyperbaric oxygen therapy be used to treat children after COVID-19? A bibliographic review. Int J Environ Res Public Health. 2022;19:15213. doi:10.3390/ijerph192215213, https://pubmed.ncbi.nlm.nih.gov/36429932/

21. Ortega MA, Fraile-Martinez O, García-Montero C, et al. A general overview on the hyperbaric oxygen therapy: applications, mechanisms and translational opportunities. Medicina (Kaunas). 2021;57:864. doi:10.3390/medicina57090864, https://pmc.ncbi.nlm.nih.gov/articles/PMC8465921/
22. Resanović I, Zarić B, Radovanović J, et al. Hyperbaric oxygen therapy and vascular complications in diabetes mellitus. Angiology. 2020;71:876-85. doi:10.1177/0003319720936925, https://pubmed.ncbi.nlm.nih.gov/32638622/
23. Sen S, Sen S. Therapeutic effects of hyperbaric oxygen: integrated review. Med Gas Res. 2021;11:30-3. doi:10.4103/2045-9912.310057, https://pubmed.ncbi.nlm.nih.gov/33642335/
24. Tambasco D, Albanese R, Tomaselli F, et al. The present and future role of hyperbaric oxygen therapy in plastic surgery. Aesthetic Plast Surg. 2025;49:1583-4. doi:10.1007/s00266-024-03867-9, https://pubmed.ncbi.nlm.nih.gov/38360957/
25. Tanaka H, Rees J, Zhang Z, et al. Emerging indications for hyperbaric oxygen treatment: registry cohort study. Interact J Med Res. 2024;13:e53821. doi:10.2196/53821, https://pubmed.ncbi.nlm.nih.gov/39078624/
26. Tian M, Du W, Yang S, et al. Application and progress of hyperbaric oxygen therapy in cardiovascular diseases. Med Gas Res. 2025;15:427-34. doi:10.4103/mgr.MEDGASRES-D-24-00107, https://pmc.ncbi.nlm.nih.gov/articles/PMC12054664/
27. Wang H, Li Y, Shen S, et al. Hyperbaric oxygen therapy for paroxysmal sympathetic hyperactivity syndrome after brain injury: a multicenter, retrospective cohort study. Med Gas Res. 2025;15:327-31. doi:10.4103/mgr.MEDGASRES-D-24-00077, https://pubmed.ncbi.nlm.nih.gov/39829168/
28. Wang P, Huang Q, Liu B, et al. Oxygen therapy in the intensive care unit. Med Gas Res. 2025;15:478-87. doi:10.4103/mgr.MEDGASRES-D-24-00143, https://pubmed.ncbi.nlm.nih.gov/40300883/
29. Yeh HT, Lee CH. Hyperbaric oxygen therapy research: an analysis of the 100 most-cited publications from 2011 to 2020. Undersea Hyperb Med. 2022;49:519-32. doi:10.22462/07.08.2022.11, https://pubmed.ncbi.nlm.nih.gov/36446297/
30. Zhang Z, Zhang W, Xu Y, et al. Efficacy of hyperbaric oxygen therapy for diabetic foot ulcers: an updated systematic review and meta-analysis. Asian J Surg. 2022;45:68-78. doi:10.1016/j.asjsur.2021.07.047, https://pubmed.ncbi.nlm.nih.gov/34376365/
31. Zilberman-Itskovich S, Catalogna M, Sasson E, et al. Hyperbaric oxygen therapy improves neurocognitive functions and symptoms of post-COVID condition: randomized controlled trial. Sci Rep. 2022;12:11252. doi:10.1038/s41598-022-15565-0, https://pubmed.ncbi.nlm.nih.gov/35821512/