UNDERSEA & HYPERBARIC MEDICINE

International Multicenter Registry for Hyperbaric Oxygen Therapy: Results through June 2021

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ABSTRACT

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Introduction: The International Multicenter Registry for Hyperbaric Oxygen Therapy (International Report Registered Identifier DERR1-10.2196/18857) was established in 2011 to capture outcomes and complications data for both Undersea and Hyperbaric Medical Society (UHMS) approved and selected unapproved hyperbaric oxygen (HBO_2) therapy indications.

Methods: A Research Electronic Data Capture (REDCap) template was designed and distributed to all participating centers for prospective data collection. Centers contributed deidentified demographic, treatment, complications, and outcome data. This report provides summary data on sites and enrollment, as well as pre- and post-treatment data on quality of life (EQ-5D-5L questionnaire), head and neck radiation outcomes, non-healing wounds (Strauss score), and idiopathic sudden sensorineural hearing loss. Data were analyzed mainly using the Wilcoxon signed-rank test.

Results: Twenty-two centers contributed data for 2,880 patients. The most common UHMS-approved indication was delayed radiation injury, followed by enhancement of wound healing, and carbon monoxide poisoning. One hundred and twenty-five patients were treated for non-UHMS approved indications. Quality of life, head and neck radiation symptoms, Strauss wound scores, and hearing were significantly improved after HBO_2. Complication rates were low and comparable to previous reports. The registry also offered the ability to analyze factors that affect outcomes, such as smoking and severity of hearing loss.

Discussion: The registry accrues prospective data on defined outcomes from multiple centers and allows for analysis of factors affecting outcomes. This registry does not have a control group, which is a limitation. Nevertheless, the registry provides a unique, comprehensive dataset on HBO_2 outcomes from multiple centers internationally. ∎

KEYWORDS: hyperbaric medicine; hyperbaric oxygen therapy; pulmonary function

INTRODUCTION

Currently hyperbaric oxygen (HBO_2) therapy is approved by the Undersea and Hyperbaric Medical Society (UHMS) to treat 14 different conditions. Data supporting the use of HBO_2 in these conditions can range from level A evidence, supported by multiple randomized controlled trials and meta-analysis data, to level C, supported by limited data or expert opinion. Use of HBO_2 for carbon monoxide poisoning, enhancement of healing in problem

wounds, and idiopathic sudden sensorineural hearing loss (ISSNHL) are supported by level A evidence, while all other indications are supported by levels B and C evidence. Multiple reasons exist for the limited supporting evidence for HBO_2. Certain indications, such as intracranial abscess or air embolism, may be seen infrequently by individual centers, making these indications difficult to study.

Additionally, common indications such as delayed radiation injury and enhancement of healing in selected problem wounds require a large commitment in time and effort by both patient and facility that make sham-controlled trials problematic. Enrolling and treating enough patients to study a particular indication at any one center presents a challenge to executing large studies. In 2001, ethicists Chan and Brody argued for the importance of patient registries in hyperbarics as a means of evaluating off-label uses of hyperbarics and defining populations in whom a clinical trial might be warranted [1].

The International Multicenter Registry for Hyperbaric Oxygen Therapy (MRHOT) was started in 2011 at the Geisel School of Medicine at Dartmouth (Lebanon, New Hampshire, U.S.) to strengthen our understanding of HBO_2's impact and to generate a large and prospective cohort detailing the outcomes of treatment. A consortium agreement in 2016 joined Dartmouth-Hitchcock Medical Center with Elliot Hospital (Manchester, New Hampshire, U.S.) as the first centers in the registry consortium. The Wesley Center for Hyperbaric Medicine (Auchenflower, Queensland, Australia) joined in 2017. In 2019 several additional centers joined the registry consortium and started entering data (Figure 1). The registry uses a uniform Research Electronic Data Capture (REDCap) template at all centers for entry of de-identified data on patients, their indications for HBO_2, and specific outcome measurements for each indication. Details of the registry design have been reported elsewhere [2]. In this review, we report the enrollment of the centers in the registry, the number of patients enrolled by indication, and selected outcomes related to quality of life, radiation injury, problem wounds, and ISSNHL. We also report on the complications experienced by patients during or after HBO_2.

METHODS

The organization and data collected within the registry have been described previously [2]. Briefly, centers join the registry by signing a consortium agreement which includes language about data sharing, publications from the data, intellectual property, liability, insurance, and confidentiality. All centers obtain Institutional Review Board (IRB) and ethics approval. Patient consent is obtained or the IRB at the enrolling site waives patient consent. Data are entered into REDCap for each patient. Centers state that they will enter data for at least 95% of the patients seen and sign a certification that they have entered all patient data once per quarter.

We then analyze the data for outliers and inappropriate data types reported in order to ensure data accuracy. Not all data collection instruments have been in the registry since its inception. The EQ-5D-5L quality of life questionnaire, for example, was added to the registry template in October 2018. Most of the questionnaires are available in Spanish as well as English. The steering committee for the registry can add or modify data collection instruments based on feedback from centers.

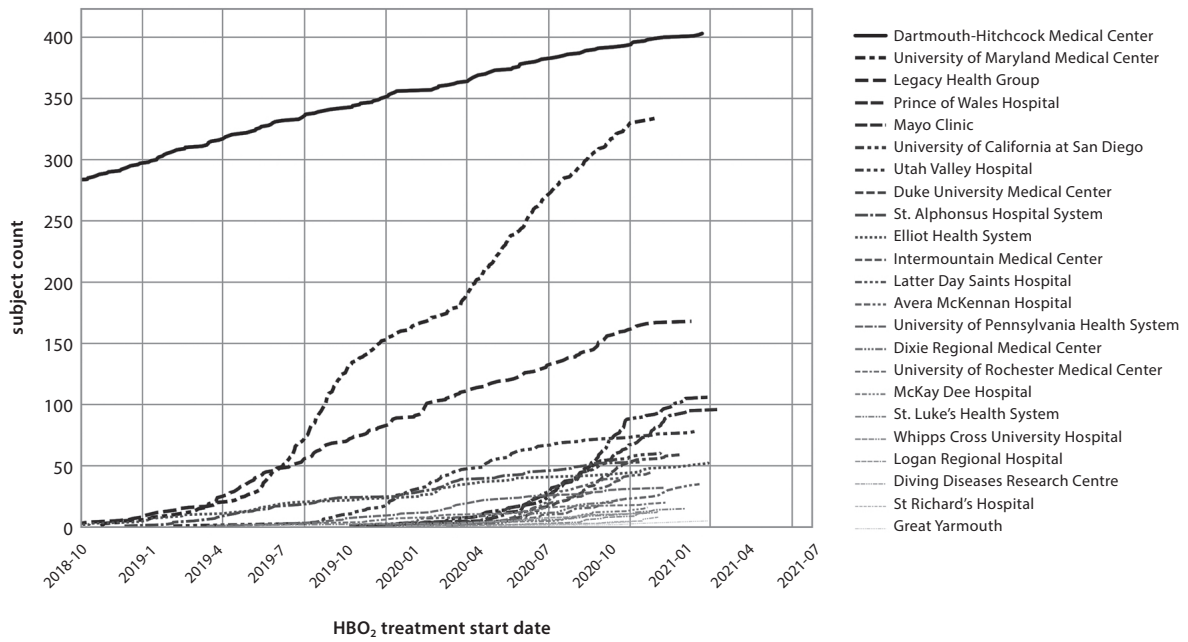
Statistical methods

The primary statistical test used thus far has been the Wilcoxon signed rank test, which is used to compare questionnaire scores, pure-tone averages, and other readings before and after HBO_2 treatment.

RESULTS

The first patient was enrolled September 6, 2011. From then to June 1, 2021, there have been 2,880 patient entries, 1,773 patients who started treatment, 1,708 patients who completed treatment, and a total of 30,577 treatments recorded. Not all enrolled sites have started entering data, as noted in Table 1. A total of 196 patients had reasons recorded for not being treated. Of these, 25 percent

Figure 1. Patient recruitment by site since 2019



At present, the three largest contributors to the registry are Dartmouth-Hitchcock Medical Center, the University of Maryland, and Legacy Health Group.

of patients were not treated because they did not meet UHMS criteria, 9.7% of patients had a contraindication to treatment, 8.7% of patients did not have a Wagner Grade 3 ulcer, and 56.6% were not treated for a reason not listed. These "other" reasons included onset of hearing loss greater than four weeks before referral, active cancer or workup for cancer, and wound healing without HBO_2.

Delayed radiation injury was the most common indication for treatment, followed by enhancement of healing in selected problem wounds and carbon monoxide poisoning (Table 2). Overall, the most commonly used treatment pressure was 2.4 ATA (Figure 2). The numbers of patients with complete data for each indication varies because of differences in implementation of various questionnaires at each center, particularly as centers started data collection and learned to work with the registry. Patient numbers also vary due to data incompleteness attributable to patients ending treatment early and patients still undergoing treatment at the time of data submission. The "Consent" variable was added later in data collection, but once it was added, only one patient did not consent to their information being used in the registry, while 2,069 consented.

Quality of life outcomes

For the 464 patients who completed both the pre- and post-HBO_2 EQ-5D visual analog scale, patient quality of life improved significantly after hyperbaric treatment ($p<0.001$, Figure 3), from a mean of 69.2 (95% confidence interval 67.3-70.9) to a mean of 75.6 (95% CI 74.0-77.2), with 0 being the worst quality of life imaginable, and 100 being the best. The visual analog scale showed improvement for 59% of the 464 patients; 22% of the cases showed a decline on this measure (Figure 3). Visual analog scales improved in every different indication treated (Table 3).

Table 1. Participating sites and locations entering data in the Multicenter Registry

Avera McKennan Hospital, Sioux Falls, SD (AVERA) – Started 11/22/19
Dartmouth-Hitchcock Medical Center, Lebanon, NH (DHMC) – Started 05/28/11
DDRC Healthcare, Hyperbaric Medical Centre, Plymouth, UK (DDRC) – Started 3/01/2021
The Diver Clinic, Poole, UK – Pending Start
Dixie Regional Medical Center, St. George, UT (DRMC)* – Started 12/31/19
Duke University Medical Center, Durham, NC (DUKE), – Started 12/21/19
East of England – LHM Hyperbaric Unit, James Paget University Hospital, Great Yarmouth (EOE) – Started 3/01/2021
Elliot Health System, Manchester, NH (EHS) – Started 05/09/18
Hyperbaric Medicine Unit, St Richard's Hospital, Chichester, UK (CHI) – Started 3/01/2021
Intermountain Medical Center, Salt Lake City, UT (IMC)* – Started 04/04/20
Latter Day Saints Hospital, Salt Lake City, UT (LDSH)* – Started 11/07/19
Legacy Health Group, Portland, OR (LHG) – Started 03/03/18
Logan Regional Hospital, Logan, UT (LMRC)* – Started 01/21/20
Mayo Clinic, Rochester, MN (MAYO), – Started 11/09/19
McKay Dee Hospital, Ogden, UT (MKD)*, Started 02/05/20
Midlands Diving Chamber, Rugby, UK – Pending Start
North England Medical and Hyperbaric Services, Hull, UK – Pending Start
Northwest Recompression Unit, Birkenhead, UK – Pending Start
Prince of Wales Hospital, Randwick, NSW, Australia (PWH) – Started 12/26/2019
St. Alphonsus Hospital System, Boise, ID (SAHS)) – Started 12/05/2018
St. Luke's Health System, Boise, ID (SLHS) – Started 03/19/20
The Hyperbaric Unit, Whipps Cross University Hospital, London, UK (LHM) – Started 3/01/2021
University of California at San Diego, San Diego, CA (UCSD) – Started 02/16/19
University of Maryland Medical Center, Baltimore, MD (UMMC) – Started 10/30/18
University of Pennsylvania Health System, Philadelphia, PA (UPENN) – Started 04/07/19
University of Rochester Medical Center, Rochester, NY (URMC) – Started 04/10/19
Utah Valley Hospital, Provo, UT (UVH)* – Started 01/01/20
Wesley Hyperbaric, Auchenflower, AU – Pending Start

*Indicates part of Intermountain Health Care System. Dates indicate when the center started data entry.

Figure 2. Most commonly used treatment pressures

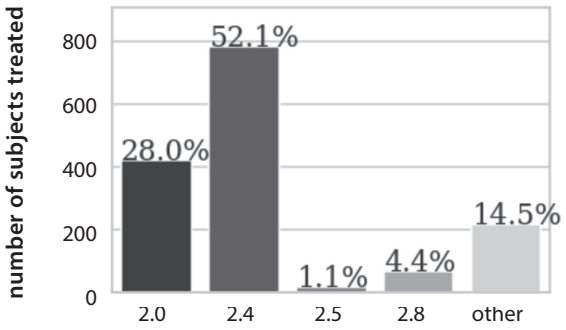
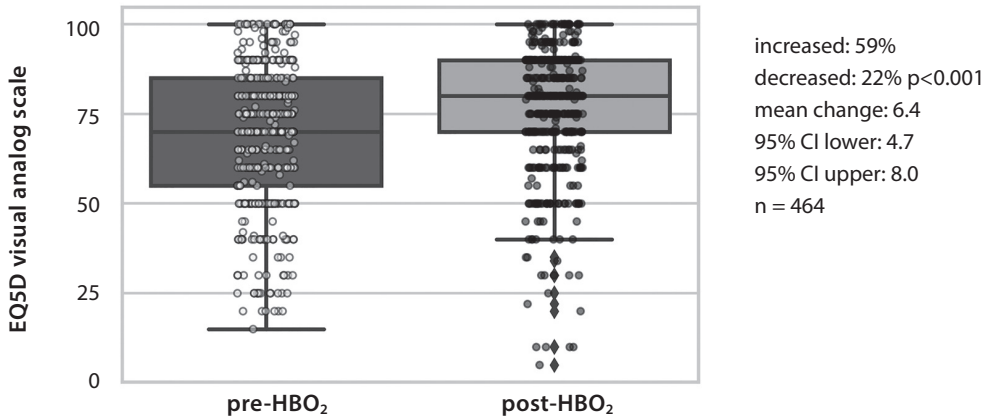


Table 2. Number of patients treated under each indication

indication	number	%
delayed radiation injury (not compromised grafts/flaps)	684	32.1
enhancement of healing in selected problem wounds (not compromised grafts/flaps)	322	15.1
carbon monoxide	306	14.4
compromised grafts and flaps	187	8.8
necrotizing soft tissue infections	173	8.1
other non uhms indication	109	5.1
osteomyelitis, refractory	97	4.6
idiopathic sudden sensorineural hearing loss	68	3.2
research protocol	45	2.1
central retinal artery occlusion	31	1.5
acute ischemia (not crush injury or compartment syndrome)	29	1.4
decompression sickness	26	1.2
crush injury, compartment syndrome	22	1
air or gas embolism (not to extremities)	19	0.9
gas gangrene	6	0.3
intracranial abscess	4	0.2
acute thermal burn injury	2	0.1
severe anemia	1	0

Figure 3. Post-HBO_2 quality of life



There was significant improvement in the EQ-5D visual analog slider measure of quality of life after HBO_2. On the EQ-5D visual analog scale, 100 represents the best quality of life imaginable and 0 the worst.

Table 3. EQ-5D visual analog scales improved across all indications treated (where 0 represents the worst quality of life and 100 represents the best)

indication	EQ-5D visual analog scale change from before to after HBO_2 (N)
acute ischemia (not crush injury or compartment syndrome)	6.2 (5)
carbon monoxide	12.4 (14)
central retinal artery occlusion	50.0 (1)
compromised grafts and flaps	6.3 (47)
crush injury	12.5 (4)
decompression sickness	16.3 (11)
delayed radiation injury (not compromised grafts/flaps)	5.5 (239)
enhancement of healing in selected problem wounds (not compromised grafts/flaps)	0.2 (57)
idiopathic sudden sensorineural hearing loss	4.8 (25)
intracranial abscess	10.0 (1)
necrotizing soft tissue infections	11.3 (6)
osteomyelitis	14.1 (27)
other non-UHMS indication	12.6 (22)
research protocol	13.3 (3)

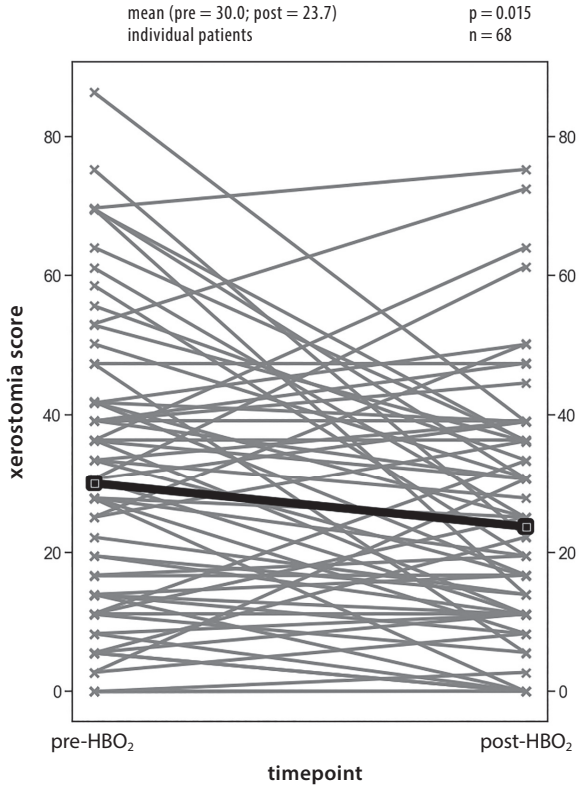
Delayed radiation injury

Delayed radiation injury (DRI) was the most common indication, with 822 patients referred. Of those referred, 709 had HBO_2 indicated with an intention to treat the person at the given center (i.e., not to be referred elsewhere). A total of 506 patients completed treatment for DRI, and the other 203 had incomplete data likely due to several factors, including patients being lost to follow-up, measures not completed at final visit, and treatment still under way at the time of data download.

The most commonly treated sites of radiation injury included the bladder (N=224), jaw/mandible (N=163), and rectum (N=71). Individuals with head and neck cancer completed a questionnaire that included questions from the EORTC QLQ H&N 35 and GRIX xerostomia questionnaires. Figure 4 shows the results from the GRIX questionnaire. Overall patients are reporting a significant improvement in xerostomia scores.

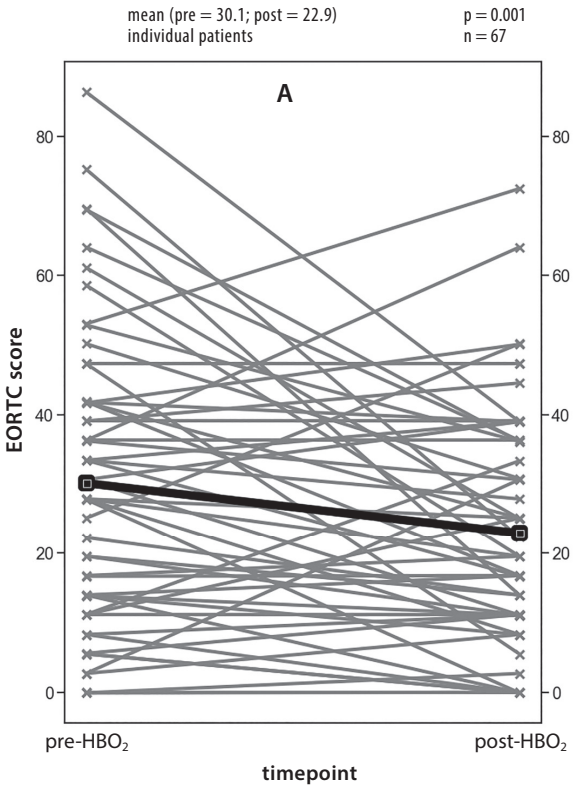
Overall, patients report improvement on the head and neck questionnaire (Figure 5). Average scores on the questionnaire dropped from 30.0 pre-HBO_2 (95% CI 25.0-35.3) to 23.7 post-HBO_2 (95% CI 19.5-28.4) (n=82, p<0.001). This change in score over the treatment period differed according to smoking status on subgroup analysis. The patients who were not smokers or had not been smoking for a year or more showed significant improvement (n=67, p<0.001)) on the head and neck questionnaire, while those who reported smoking the past year did not (n=11, p=0.14).

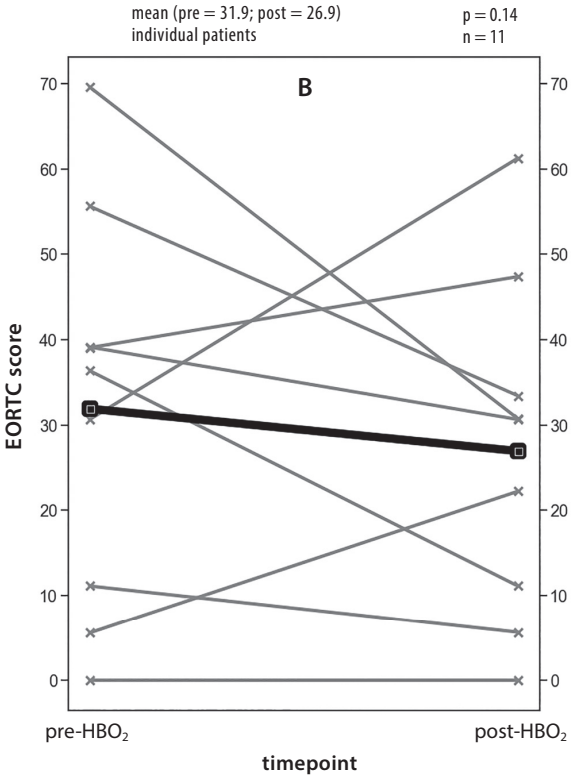
Figure 4. Xerostomia symptoms



Patients with head and neck cancer treated with HBO_2 showed significant improvement in xerostomia overall. Scores of 0 represent no symptoms, while higher scores represent more xerostomia symptoms.

Figure 5: Smokers vs. non-smokers





Figures 5A-B – right column ▶
Patients who are former smokers or non-smokers had a significant improvement in their symptoms: 5A top, p<0.001, n = 67, 49% of cases improved compared to 39% whose EORTC score worsened.

Patients who were current smokers or who quit in the last year did not have significant improvement in their symptoms as reported by the head and neck questionnaire (5B bottom, p = 0.14, n = 11). Lower EORTC scores represent fewer patient-reported symptoms.

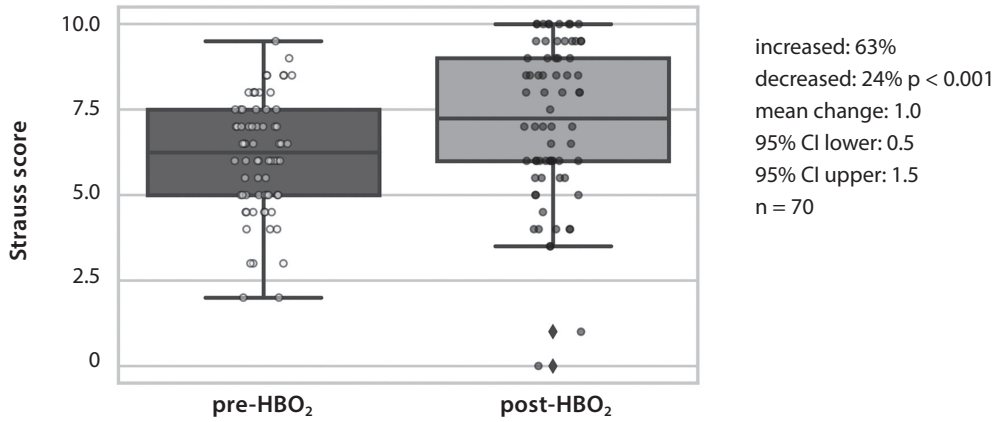
Enhanced healing in selected problem wounds

A total of 517 patients were evaluated for treatment for enhancement of healing in selected problem wounds. For 326 of these patients HBO_2 was indicated and the patient was going to be treated at the center doing the evaluation. Of those, 231 had completed HBO_2 at the time of this report. Of these patients 120 had diabetic foot wounds, 100 were listed as "other (cannot be compromised graft or flap)," and seven were diabetic wounds in locations other than the foot. The "other" wounds included two wounds from pyoderma gangrenosum, two wounds related to critical limb ischemia, two wounds related to CREST syndrome, four wounds related to surgery, including knee replacement, amputation, and penile implant. Because the Strauss measure was only recently added to the REDCap template, only 71 patients had pre- and post-HBO_2 Strauss scores recorded. Of those, 63% showed improvement on the Strauss Score and 24% worsened. In diabetic foot wounds, the Strauss score improved significantly from a median of 6.25 (range 2-9.5) pre-treatment to 7.25 (range 0-10) post-treatment ($p<0.001$, Wilcoxon signed-rank test).

Idiopathic sudden sensorineural hearing loss

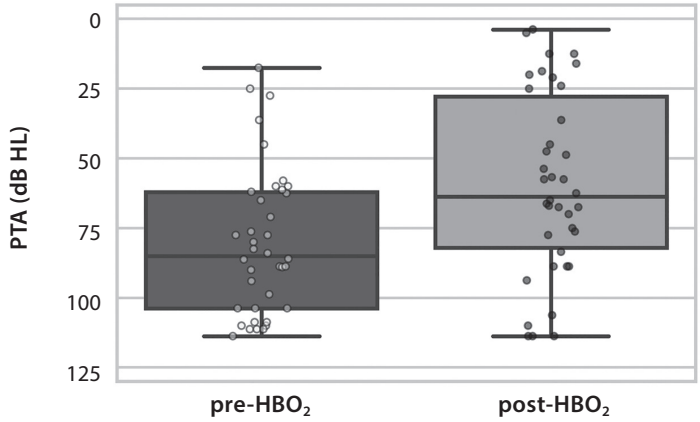
One hundred eighteen patients were referred for idiopathic sudden sensorineural hearing loss (IS-SNHL). Of these, 84 received a formal evaluation/consultation and 83 had HBO_2 indicated. Of those, 11 declined treatment and four were treated at a different center, leaving 68 patients who were treated. For the 38 patients with hearing test data before and after HBO_2, the four-frequency pure-tone average (500, 1,000, 2,000, 4,000 Hz averaged from the audiogram) improved significantly from 80.2 dB (95% CI 71.8-88.5) to 59.4 dB (95% CI 49.0-69.8) after HBO_2 ($p<0.001$, Wilcoxon signed-rank test, Figure 7). Seventy-six percent of the patients had improved PTA values following HBO2 while 16% had worsening in PTA. Nineteen patients had word recognition scores (WRS) before and after HBO_2. WRS improved significantly after HBO_2, with the mean percent correct increasing from 26.5% to 53.5%, a change of 26.9%, (95% CI 13.9% - 44.1% Figure 8). WRS improved for 53% of the 19 patients and none of the patients had a worse WRS after treatment. For the patients treated from 0-14 days after their hearing loss, there was a significant improvement in pure-tone average ($p<0.001$, N=23, 87% of subjects improved), while patients treated after 14 days had less significant improvement ($p=0.019$ N=15, 60% of patients improved, Figure 9).

Figure 6. Enhanced healing in select problem wounds



The Strauss score improved significantly after HBO_2, from a mean of 6.1 (95% CI 5.8-6.5) to 7.2 (95% CI 6.6-7.7). Strauss scores of 0-3 represent "futile" wounds, 4-7 represent "problem" wounds, and scores of 8-10 represent "healthy" wounds.

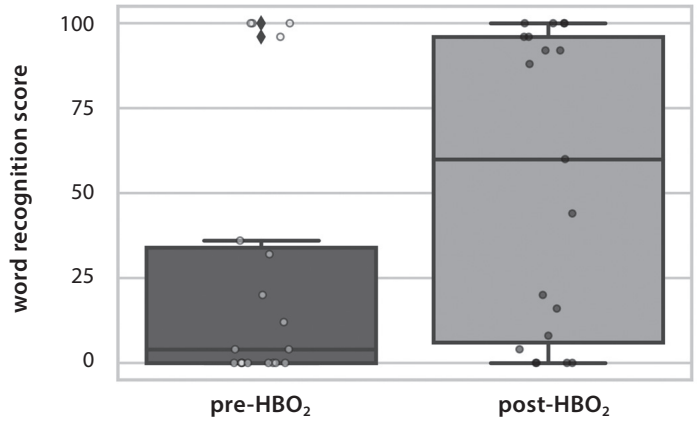
Figure 7. Pure-tone hearing averages



increased: 16%
decreased: 76% p<0.001
mean change: -20.8
95% CI lower: -28.6
95% CI upper: -14.6
n = 38

Pure-tone average (PTA) improved significantly after HBO_2 (mean PTA 80.2 dB HL pre-treatment, 59.4 dB HL post-treatment). Pure-tone hearing average of <25 dB represents normal hearing, while >95 dB represents profound hearing loss.

Figure 8. Word recognition scores

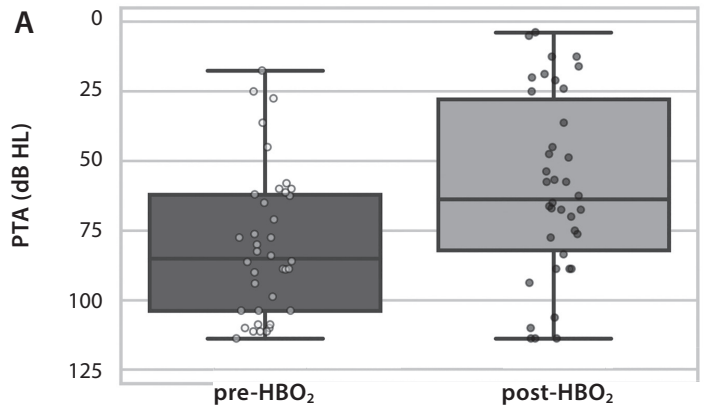


increased: 53%
decreased: 0% p = 0.005
mean change: 26.9
95% CI lower: 13.9
95% CI upper: 44.1
n = 19

Complications

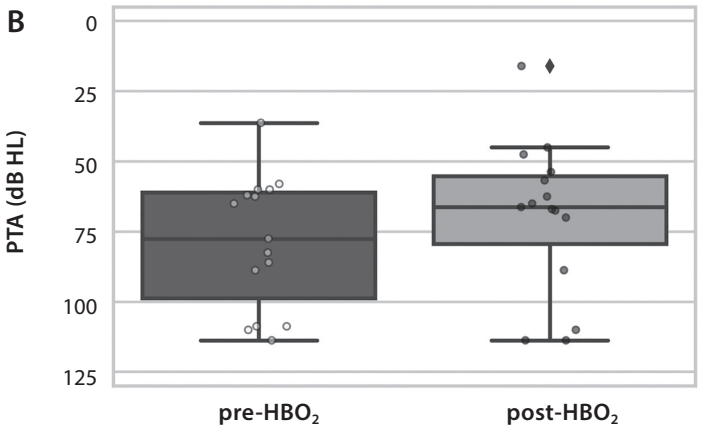
Complications are reported from the 1,773 patients who have started treatment. When difficulties arise with equalization of middle ear pressure, patients are sometimes referred to the ear, nose and throat (ENT) service for evaluation for myringotomy or pressure-equalization tubes (ear tubes). One hundred fifty-four (8.7%) patients were evaluated by ENT for middle ear barotrauma (MEBT), and 91 (5.1% of all patients) had an intervention in order to proceed with hyperbaric treatments. Thirty-three patients (1.9%) had unilateral ear tubes, and 49 (2.8%) had bilateral ear tubes placed. Nine (0.51%) had unilateral myringotomies. Of the patients with otic barotrauma, 42.9% were in monoplace chambers for more than 90% of their treatments, and 57.1% of patients were treated in a multiplace chamber more than 90% of the time. Fifty-five (3.1%) experienced sinus barotrauma, and four (0.23%) experienced dental barotrauma.

Figure 9. Pure-tone average scores



increased: 16%
decreased: 76% p<0.001
n = 38

PTA improved in 87% of patients who received HBO_2 within 14 days of hearing loss (mean PTA 81.2 dB HL pre-treatment, 52.8 dB HL post-treatment).



increased: 27%
decreased: 60% p = 0.019
mean change: -9.1
95% CI lower: -15.6
95% CI upper: -3.9
n = 15

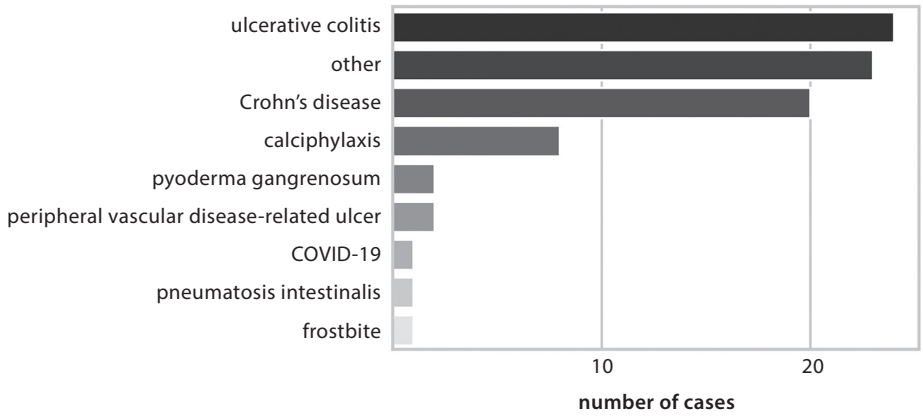
PTA improved in 60% of patients who received HBO_2 after 14 days of hearing loss (mean PTA 78.7 dB HL pre-treatment, 69.6 dB HL post-treatment).

Two (0.11%) patients developed pulmonary edema while in the chamber. One was an emergency treatment at 2.8 ATA for carbon monoxide poisoning, and the other was a non-emergency treatment at 2.0 ATA.

Seven (0.39%) patients experienced seizures, and 20 (1.1%) others had other signs of possible CNS toxicity. Three seizures occurred at treatment pressures of 2.8 ATA, and four at 2.4 ATA. The overall seizure rate was 2.3 per 10,000 treatments, with a rate of 1.1 per 100 treatments at 2.8 ATA and 1.4 per 10,000 treatments for pressures at 2.5 ATA and below. Two seizures occurred during treatment for carbon monoxide poisoning and were emergency treatments. The other seizures occurred during treatments for osteomyelitis, delayed radiation injury, compromised graft/flap, and a non-UHMS indication. There were no seizures reported at 2.0 ATA.

One hundred sixty-seven (9.4%) of patients had some confinement anxiety. Out of these patients, in 55 (3.1%) the anxiety was severe enough to stop their treatment course; 29 (1.6%) patients stopped a single treatment but were able to continue their treatment course; and 83 (4.7%) had anxiety that could be managed without interrupting treatments. Fifty-three (3.0%) patients experienced sweating excessive enough to soak the linens in the chamber. Two hundred fifteen (12.1%) patients reported visual changes during their treatment course. No pneumothoraces developed during treatment.

Figure 10. Non-UHMS indications for HBO_2 by number of cases



Inflammatory bowel disease (ulcerative colitis and Crohn's disease) makes up the greatest number of non-UHMS referrals reported in the registry.

Discussion

The registry now includes data from 22 centers, having grown substantially over the last two years. These descriptive data are important in establishing a baseline understanding of hyperbaric programs caseloads, patient characteristics, indications for treatment, outcomes, and complications of HBO_2. HBO_2 is resource-intensive both for centers and for patient,s as it involves daily two-hour treatments for up to two months, depending on the indication. For many patients, this treatment regimen can affect their employment and may involve lost wages and substantial travel costs. Despite these barriers to HBO_2, the significant net improvements in reported quality of life with this treatment are important findings that justify future observational and intervention studies to compare the impacts of HBO_2 with other forms of treatment. The international multicenter registry provides a critical infrastructure to support this kind of research.

The most commonly treated indications were delayed radiation injury and enhancement of healing in selected problem wounds. The most commonly documented non-UHMS approved indications were inflammatory bowel disease and calciphylaxis (Figure 10). The registry provides an important mechanism to study treatment outcomes for these uncommon, emerging non-UHMS approved indications because it allows the pooling of data from small numbers of patients at multiple centers, with the potential to provide adequate statistical power for meaningful analyses.

As more patient entries accumulate in the registry it becomes possible to analyze factors affecting outcomes. An example of this is shown in the analysis of the head and neck questionnaire among patients with head and neck radiation (Figure 5). When the subgroup of patients who had smoked in the last year was analyzed, these patients did not show a significant improvement in their scores on the questionnaire, while the "non-smoker" and those who had quit over one year ago, did have significant improvement. The number of smokers is limited, however, and this result may change as more patients are entered into the registry. Nevertheless, this shows the kind of analyses that can be done with the registry.

In patients with diabetic foot wounds, the Strauss score may be used to measure whether wounds fall into the "futile" (0-3), "problem" (4-7), or "healthy" (8-10) range [3]. Average wound scores improved significantly from a median of 6.25 to 7.25, indicating that for some patients their wounds progressed from being indolent "problem" wounds to a healthy, healing wound. This supports existing evidence for the use of HBO_2 in diabetic foot wounds

[4-6], but highlights the need to study predictors of better outcomes, as well as the potential benefit of earlier referral and the role of HBO_2 as part of multidisciplinary diabetic foot care. As entries in the registry expand it will be possible to analyze the factors associated with the variability in response.

The four-frequency pure-tone average and word recognition scores in patients treated for ISSNHL improved significantly on average. Consistent with what has been seen in other studies, patients treated two or more weeks out from initial hearing loss had less significant improvement in pure-tone average compared to patients who received HBO_2 within two weeks of losing their hearing [7]. As data accrue, it will be possible to quantify more precisely the clinical benefits of treatment according to the delay since symptom onset.

Previous studies have reported risk of seizure during treatment at 4.5 per 1,000 patients at a single center, or approximately 2.3 in 10,000 treatments [8]. Here, we report seven seizures in 1,773 patients across these centers and a rate of 2.3 seizures in 10,000 treatments. Notably, no seizures were reported at pressures lower than 2.4 ATA (although many more patients were treated at 2.4 ATA compared to 2.0 ATA). As noted in other studies, otic barotrauma was common, with 8.9% of patients being referred to ENT for evaluation and 5.1% having either an ear tube or myringotomy. This is somewhat higher than a 2016 study, in which 2.4% of patients required intervention for HBO_2-related otic trauma [9].

As the registry grows, it will be possible to study the effects of factors such as age, smoking history, diabetes, and specific disease characteristics on HBO_2 outcomes, and to identify patients most and least likely to benefit from treatment. For example, the results of the head and neck questionnaire in our radiation injury patients shows differences in outcomes by smoking status, which could potentially change practice patterns. The registry also offers the ability to examine practice variability and complications at different sites, prospectively identifying areas for quality improvement.

One major limitation of this registry is that patients are not randomized to HBO_2, and there are no data on untreated controls. We can report the trends of HBO_2 use around the world, demonstrate improvement among patients who do receive treatment and identify predictors of response to treatment. This infrastructure can be used as a starting point for randomized controlled trials and observational studies at participating centers. The expense of HBO_2 and small caseloads at each center contribute to the difficulty of doing such studies, and the ability to perform multicenter studies may increase patient enrollment and enhance our ability to study the less common indications for HBO_2.

As with any new registry, a major challenge is monitoring and ensuring data completeness. We are currently assessing completeness for key variables, and participating centers will be required to remediate where necessary to continue participating in the registry consortium. We have limited the number of data points required to minimize the time requirement to participate in the registry, because the data collection for the registry must take place within the framework of routine clinical operations.

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REFERENCES

1. Chan EC, Brody B. Ethical dilemmas in hyperbaric medicine. Undersea Hyperb Med. 2001 Fall;28(3):123-130. PMID: 12067147.

2. Harlan NP, Ptak JA, Rees JR, Cowan DR, et al. Development of an international, Multicenter, Hyperbaric oxygen treatment registry and research consortium: protocol for outcome data collection and analysis. JMIR Res Protoc. 2020;9(8):e18857. Epub 2020/06/25. doi: 10.2196/18857. PubMed PMID: 32579537; PMCID: PMC7459436.

3. Strauss MB, Moon H, Busch JA, Jones CK, et al. Reliability assessment of an innovative wound score. Wounds. 2016;28(6):206-213. Epub 2016/07/06. PubMed PMID: 27377611.

4. Abidia A, Laden G, Kuhan G, Johnson BF, Wilkinson AR, Renwick PM, Masson EA, McCollum PT. The role of hyperbaric oxygen therapy in ischaemic diabetic lower extremity ulcers: a double-blind randomised-controlled trial. Eur J Vasc Endovasc Surg. 2003;25(6):513-518. Epub 2003/06/06. doi: 10.1053/ejvs.2002.1911. PubMed PMID: 12787692.

5. Londahl M, Katzman P, Nilsson A, Hammarlund C. Hyperbaric oxygen therapy facilitates healing of chronic foot ulcers in patients with diabetes. Diabetes Care. 2010;33(5):998-1003. doi: 10.2337/dc09-1754. PubMed PMID: 20427683; PMCID: PMC2858204.

6. Kranke P, Bennett MH, Martyn-St James M, Schnabel A, Debus SE, Weibel S. Hyperbaric oxygen therapy for chronic wounds. Cochrane Database Syst Rev. 2015(6): CD004123. Epub 2015/06/25. doi: 10.1002/14651858.CD004123.pub4. PubMed PMID: 26106870; PMCID: PMC7055586.

7. Sherlock S, Thistlethwaite K, Khatun M, Perry C, Tabah A. Hyperbaric oxygen therapy in the treatment of sudden sensorineural hearing loss: a retrospective analysis of outcomes. Diving Hyperb Med. 2016;46(3):160-165. Epub 2016/10/11. PubMed PMID: 27723017.

8. Costa DA, Ganilha JS, Barata PC, Guerreiro FG. Seizure frequency in more than 180,000 treatment sessions with hyperbaric oxygen therapy - a single centre 20-year analysis. Diving Hyperb Med. 2019;49(3):167-174. Epub 2019/09/17. doi: 10.28920/dhm49.3.167-174. PubMed PMID: 31523791; PMCID: PMC6884101.

9. Yamamoto Y, Noguchi Y, Enomoto M, Yagishita K, Kitamura K. Otological complications associated with hyperbaric oxygen therapy. Eur Arch Otorhinolaryngol. 2016;273(9):2487-2493. Epub 2015/12/10. doi: 10.1007/s00405-015-3845-9. PubMed PMID: 26650550.

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