

# A Retrospective Analysis of Adverse Events in Hyperbaric Oxygen Therapy (2012-2015): Lessons Learned From 1.5 Million Treatments

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## ABSTRACT

**OBJECTIVE:** To describe the distribution and occurrence of adverse events recorded during hyperbaric oxygen (HBO) therapy from 2012 to 2015. In this analysis, events are defined as otic/sinus barotrauma, confinement anxiety, hypoglycemia, oxygen toxicity, pneumothorax, seizure, and shortness of breath.

**DATA AND ANALYSIS:** The data for the analysis were drawn from a proprietary electronic health data system that contained information on 1,529,859 hyperbaric treatments administered during 53,371 treatment courses from 2012 to 2015 in outpatient wound care centers across the United States managed by Healogics, Inc, Jacksonville, Florida.

**RESULTS:** Of the 1.5 million treatments included in the analysis, 0.68% were associated with an adverse event. Barotrauma and confinement anxiety were the most frequently reported events. Medically severe events were extremely uncommon, with fewer than 0.05 instances of oxygen toxicity per 1000 treatments and only 1 confirmed case of pneumothorax.

**CONCLUSIONS:** Results indicate that the occurrence of adverse events associated with HBO therapy is infrequent and typically not serious. The findings of this study suggest that when administered according to the appropriate therapeutic protocols HBO therapy is a safe and low-risk intervention.

**KEYWORDS:** adverse events, hyperbaric oxygen therapy, wound care

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HBO treatment recommend prescribed pressures ranging between 2.0 and 2.5 ATA for 90 to 120 minutes. Hyperbaric oxygen therapy is currently approved to treat a variety of conditions and is commonly used in the treatment of select chronic wounds, delayed radiation injury, and necrotizing soft tissue infections.<sup>1</sup>

Concerns of adverse patient reactions may influence treatment decisions regarding HBO therapy for eligible patients. In general, research finds that adverse event occurrence associated with HBO therapy is low and typically benign; however, the reported rates differ markedly across studies. Common events associated with HBO therapy include otic/sinus barotrauma and confinement anxiety. Although less frequent, seizures associated with oxygen toxicity and hypoglycemia have been observed. In extremely rare cases, pulmonary barotrauma has been reported.<sup>2-4</sup>

Previous analyses of adverse events associated with HBO therapy vary considerably in their findings and measurement of event occurrence.<sup>5-7</sup> At the patient level, overall adverse event incidence rates of 2% have been found, whereas per-treatment rates of 0.44% have been reported.<sup>2</sup> The most commonly studied events include barotrauma, oxygen toxicity, and confinement anxiety.<sup>2,4</sup> Chart review analyses of specific HBO-related events typically report the highest incidence for specific event types, whereas large-scale retrospective studies tend to find slightly lower rates. For example, a single-institution chart review analysis found an oxygen toxicity seizure rate of 0.17% at the treatment level,<sup>8</sup> whereas a large-scale retrospective analysis based on institutional reports found a rate of 0.03% at the treatment level.<sup>9</sup> The variability in findings is likely attributable to differences in patient selections, single-institution analysis, event definition and reporting data, and institutional protocols.

The purpose of this study is to provide an updated summary and analysis of the per-treatment adverse event incidence and to demonstrate the safety of HBO therapy. The authors used pooled data on more than 1.5 million HBO treatments that were administered in a subset of hospital outpatient specialty wound

## INTRODUCTION AND BACKGROUND

During hyperbaric oxygen (HBO) therapy, an individual breathes near 100% medical-grade oxygen intermittently while inside a hyperbaric chamber that is pressurized to greater than sea level pressure (1 atmosphere absolute [ATA], or 101.325 kPa). Current information indicates that pressurization for clinical treatments should be 1.4 ATA or higher. Clinical indications accepted for

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care centers from 2012 to 2015. Specifically, the authors assessed the distribution, correlates, and timing of event occurrence. Furthermore, although several studies have addressed the occurrence of adverse events, few have addressed the likelihood of treatment course completion after event occurrence. Thus, the authors examined the likelihood of premature termination of HBO treatment following adverse events.

## METHODS

### Data

The authors obtained data for this analysis from the proprietary electronic health data system of a specialty wound care management company (Healogics, Inc, Jacksonville, Florida). The database includes data on HBO treatments administered in outpatient wound care centers from 2012 to 2015. Information regarding the individual treatment characteristics, the therapeutic course, and the patient admission was recorded.

### Study Design

This is a retrospective study conducted using data from multiple advanced wound care and hyperbaric medicine centers across the United States. Patients were treated under the Undersea and Hyperbaric Medicine—or the Centers for Medicare & Medicaid Services—approved indications using evidence-based guidelines for the number, depth, duration, and frequency of treatments delivered by trained HBO technicians under physician supervision. The majority of treatments were administered for wound-related indications. Information and characteristics of the treatment, treatment course, and patient were recorded at the point of care.

All HBO treatments administered from 2012 through mid-June 2015 were eligible to be included in the analysis. Treatments with missing or data entry errors on key study elements (3687 treatments) were excluded from the analysis, resulting in a final sample size of 1,529,859 treatments and 53,371 treatment courses. The secondary data used for the analyses were aggregated to the treatment and treatment course level. No identifiable patient-level data or identifiers were included in the analyses; thus, the study was exempt from review by the institutional review board.

### Adverse Events

During or after the HBO treatment, an adverse event may be observed by the HBO technician, or the patient may report symptoms indicative of an adverse event. Depending on the event, the HBO technician follows a policy-driven response that involves notifying the supervising physician. This individual may alter or elect to terminate the treatment.

Treatment-associated events are defined as an occurrence identified by prior clinical literature as being associated with the HBO therapy.<sup>3</sup> Events include otic/sinus barotrauma, confinement anxiety, hypoglycemia, oxygen toxicity, seizure, shortness of breath, and pneumothorax. For this study, barotrauma is defined as a complication of pressure equalization of the middle ear or sinus. The patient typically reports pain in association with an inability to clear or equalize pressure in the ears. Confinement anxiety is identified when a patient inside a chamber verbalizes or signals the desire to end treatment because of claustrophobia. Hypoglycemia without an associated seizure event is identified as a blood glucose level less than 70 mg/dL as measured by a calibrated glucometer immediately after HBO treatment on patients with diabetes. Oxygen toxicity without associated seizure is the effect on the central nervous system of oxygen overdosage. Clinical staff are trained to identify the following signs and symptoms of oxygen toxicity: blurred or tunneled vision, irritability (ie, a marked change in behavior), nausea, facial twitching, ringing or roaring sound in ears, and dizziness. Typically, seizure in relation to HBO therapy is a manifestation of oxygen toxicity or hypoglycemia and/or a preexisting medical condition. Patients who progress to a seizure frequently experience a transient loss of consciousness and convulsions. For the purpose of this article, the authors distinguish among symptomatic oxygen toxicity and hypoglycemia and seizure events. Shortness of breath is identified via patient complaint. Finally, pneumothorax is defined as air in the plural space as a result of alveolar disruption and pulmonary barotrauma. Patients may complain of sudden chest pain with or without shortness of breath.

### Data Collection Procedures

Data on individual HBO treatments are entered by the HBO technician as care is administered. Data on treatment course characteristics and patient diagnoses are collected by clinical staff and entered into a proprietary electronic health data system designed for advanced wound care and hyperbaric medicine. All data were extracted using Structured Query Language. All subsequent analyses were conducted in Stata 14 (StataCorp LP, College Station, Texas).

### Statistical Analyses

The analyses consist of 2 parts. First, the authors provide descriptive and bivariate analyses of event occurrence during or after HBO treatments. Characteristics of the individual treatment, treatment course, and patient are provided. The authors use  $X^2$  tests for categorical variables and  $t$  tests for continuous measures. They use Kaplan-Meier curves to demonstrate the treatment time in minutes by the presence of an event during the treatment.

Binary logistic regression is used for predicting the odds of premature termination of the treatment course by event type.

## RESULTS

### Treatment Level

During individual HBO treatments, adverse events were extremely infrequent (Table 1). During 99.3% of all HBO treatments, no adverse event was recorded. The most frequently occurring event was otic/sinus barotrauma (0.37%), followed by confinement anxiety (0.16%) and symptomatic hypoglycemia (0.08%). More serious events, such as seizure (0.02%) and oxygen toxicity without associated seizure (0.01%), occurred very rarely. Only 1 instance of confirmed pulmonary barotrauma was identified out of 1.5 million treatments. Table 2 displays the summary statistics for treatments with and without an event. On average, treatments with a recorded event were significantly shorter than those without an event. Additional information on pressure-reached data was available for a subsample of 814,346 treatments (Table 3). Categories in this data set include standard treatment depth values, as well as a category to capture treatments that did not achieve prescribed pressure. On average, the percentage of treatments with an event was associated with higher pressure-reached values. For example, 18.8% of treatments with an event had a pressure-reached value of 2.5 ATA compared with 15.2% of treatments without an event. In addition, treatments with event occurrence were less likely to have reached the prescribed pressure level.

### Kaplan-Meier Curves

Figure 1 provides the Kaplan-Meier curves for treatment time recorded in minutes. In general, treatments with an event had a recorded treatment time that was significantly shorter than those without an event. The data did not allow for a determination of the exact cause of treatment termination (ie, whether the treatment was discontinued prematurely because of event occurrence);

**Table 2.**

### MEANS AND PERCENTAGES FOR HYPERBARIC OXYGEN TREATMENTS BY EVENT OCCURRENCE<sup>a</sup>

Variable	No Event		Event		P
	Mean/%	SD	Mean/%	SD	
Treatment length, min	113.40	14.19	70.95	44.92	.00
Age, y	62.63	13.30	60.20	13.62	.00
Female, %	36.73	—	34.90	—	.00

N = 1,529,859.

<sup>a</sup>t test for continuous variables,  $\chi^2$  for categorical variables.

however, the mean treatment time for treatments with an event was significantly less than the average nonevent treatment length value. Thus, the authors use treatment length as a proxy for time to event occurrence.

### Treatment Course

Findings for the analysis of treatment course are presented in Table 4. For those treatment courses with an event occurrence, an average 1.39 (SD, 0.91) events were recorded. The mean treatment length per course was 7.7 minutes greater ( $P < .001$ ) for treatment courses without an event occurrence. The percentage of ordered treatments that were completed was significantly lower for therapeutic courses with event occurrence. Approximately 70% of treatments ordered were completed during courses without an event, whereas only 65% were completed among those with event occurrence. Table 5 presents the diagnosis associated with the treatment course by event occurrence. Hyperbaric therapy for the treatment of diabetic ulcers had a significantly higher event occurrence rate relative to all additional diagnoses, as did treatments administered for indications captured in the "other" category. Diagnoses in the "other" category include decompression illness, cyanide poisoning, thermal burns, idiopathic sudden

**Table 1.**

### HYPERBARIC OXYGEN TREATMENTS, ADVERSE EVENTS, AND MEAN TREATMENT LENGTH 2012–2015

	n	Percentage	Rate per 10,000	Mean Treatment Length (min)	SD
No event	1,519,419	99.32	9,931.76	113.35	14.06
Barotrauma <sup>a</sup>	5643	0.37	36.88	64.04	51.87
Confinement anxiety	2436	0.16	15.92	64.27	31.88
Hypoglycemia	1275	0.08	8.33	103.75	19.11
Seizure	267	0.02	1.74	99.54	26.82
Shortness of breath	739	0.05	4.83	79.72	32.30
Oxygen toxicity	79	0.01	0.52	96.04	27.68
Pneumothorax	1	0.00	0.00	—	—
Total	1,529,859	100	10,000	113.06	14.91

<sup>a</sup>otic or sinus.

**Table 3.**

**ATMOSPHERIC PRESSURE REACHED DURING TREATMENT BY PRESENCE OF EVENT**

Pressure Reached	No Event		Event		Total
	Mean	SD	Mean	SD	
2.0 ATA	603,770	75.59	3466	70.21	607,236
2.4 ATA	81,304	10.04	431	8.73	81,735
2.5 ATA	123,285	15.23	928	18.81	124,213
Other <sup>a</sup>	1050	0.13	112	2.27	1162
Total	809,409	100	4937	100	814,346

N = 814,346  
 $\chi^2, P < .001$

<sup>a</sup>A small subset of treatments was recorded outside prescribed pressure reached levels likely because of treatment termination. These values are coded as other ATA. Abbreviation: ATA, atmosphere absolute.

**Table 4.**

**MEANS AND PERCENTAGES FOR HYPERBARIC OXYGEN TREATMENT COURSE<sup>a</sup> BY PRESENCE OF EVENT**

Variable	No Event		Event		P
	Mean	SD	Mean	SD	
No. of complications			1.39	0.91	—
Average course treatment length, min	112.41	13.92	104.67	23.28	.000
Percent of treatment completed	70.04	33.90	65.47	34.97	.000

n = 53,371.

<sup>a</sup>t test for continuous variables;  $\chi^2$  for categorical variables.

(95% confidence interval, 2.01–4.32) and 2.72 (95% confidence interval, 2.36–3.25), respectively.

**DISCUSSION**

The primary aim of this analysis was to describe the distribution and characteristics of HBO treatment–associated adverse events. The findings indicate that event occurrence is extremely rare and typically of low medical severity. The overall adverse event rate at

**Table 5.**

**PERCENTAGES OF DIAGNOSES ASSOCIATED WITH HYPERBARIC OXYGEN TREATMENT COURSE BY PRESENCE OF EVENT**

Diagnosis	No Event	Event	Total
Diabetic ulcer	18,038	3422	21,460
	39.50	44.41	40.21
Compromised graft/flap	6264	365	6629
	13.72	4.74	12.42
Radionecrosis	9024	810	9834
	19.76	10.51	18.43
Chronic refractory osteomyelitis	8403	159	8562
	18.40	2.06	16.04
Acute carbon monoxide	219	6	225
	0.48	0.08	0.42
Acute traumatic peripheral ischemia	535	12	547
	1.17	0.16	1.02
Arterial embolism and thrombosis	964	14	978
	2.11	0.18	1.83
Crush injury	690	14	704
	1.51	0.18	1.32
Gas gangrene	143	1	144
	0.31	0.01	0.27
Necrotizing fasciitis	761	26	787
	1.67	0.34	1.47
Other	624	2877	3501
	1.37	37.33	6.56
Total	45,665	7706	53,371
	100.00	100.00	100.00

n = 53,371.

$\chi^2, P < .001$ .

sensorineural hearing loss, and other diagnoses captured as free-text fields in physician notes.

Table 6 presents the odds of premature treatment course termination by event type. Because of the low sample size, oxygen toxicity was excluded from the model. Treatment courses without an event were the reference category. Relative to treatment courses without an occurrence, courses with adverse events had significantly higher odds of premature treatment discontinuation. Treatment courses that recorded shortness of breath and confinement anxiety had the highest odds of early termination compared with treatment courses without an event: 2.74

**Figure 1.**  
**TREATMENT TIME BY EVENT TYPE**

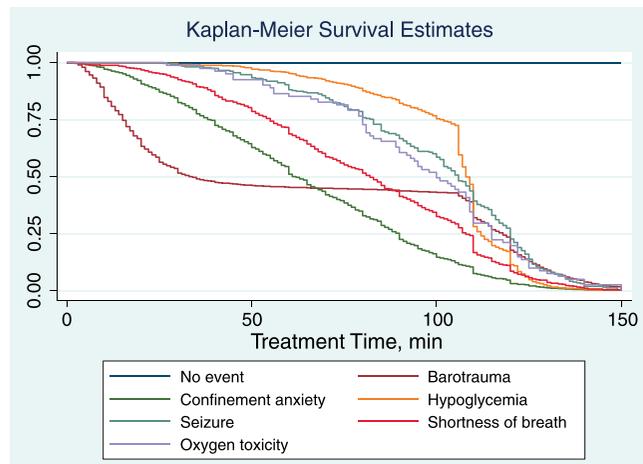


Table 6.

**ODDS OF DISCONTINUING TREATMENT COURSE**

	Odds Ratio	SE	95% Confidence Interval	
Barotrauma	1.38	0.08	1.27	1.55
Confinement anxiety	2.72	0.23	2.36	3.25
Hypoglycemia	1.81	0.48	0.98	2.65
Seizure	2.39	0.93	1.26	5.71
Shortness of breath	2.74	0.58	2.01	4.32
Constant	0.41	0.00	0.39	0.41

Pseudo  $R^2 = 0.0035$ . Likelihood ratio  $\chi^2 = 235.01$ ;  $P < .000$ .  $n = 53,371$ .

the treatment level was 0.68%. Barotrauma and confinement anxiety are most likely to occur, with more severe events such as seizure or oxygen toxicity without seizure occurring in less than 2 of every 10,000 treatments administered.

In general, treatments associated with an adverse event were shorter than those without, indicating that when an event is registered a treatment is more likely to be ended early. Treatments during which a patient complained of barotrauma and confinement anxiety had the shortest mean duration of just over an hour, suggesting these occurrences happen earlier during the treatment.

Female patients were less likely to have an event during treatments. Prior research demonstrates gender differences in health-care utilization behaviors; women are more likely to use preventive services and to seek care early in the disease process.<sup>12,13</sup> Thus, female patients may experience fewer severe comorbid conditions and may be more likely to adhere to other prescribed treatments, reducing the likelihood of treatment complications. In addition, treatments with an event occurrence were more commonly observed with higher pressure values, validating previous findings that the risk of event occurrence is increased with greater pressure.<sup>2,8</sup> Patients who experienced an event typically had slightly more than 1 event per treatment course. Individuals who reported an event completed a significantly lower percentage of the treatments ordered by the physician and were more likely to discontinue the therapeutic course. The occurrence of confinement anxiety and shortness of breath were associated with the highest odds of discontinuing treatment. Therefore, providers may improve treatment completion rates through enhanced patient communication, identification of those at risk of claustrophobia, and initiating appropriate prophylactic measures.

**LIMITATIONS**

The current analysis is limited to data captured by a proprietary electronic health data system that was designed for the purpose of clinical decision making rather than retrospective research. In

a prior analysis conducted by Diversified Clinical Services, which is now part of Healogics, Inc, the authors found a per-treatment adverse event rate of 0.40% using similar data from 2009 to 2010.<sup>11</sup> Through improvements in data capture and provider education, the authors believe the current findings represent a more accurate depiction of adverse event occurrence associated with HBO therapy.

It is important to note that this analysis is limited to reported and recorded events. More than 400 distinct outpatient care centers were included in the analysis, and variation is likely in the quality of data capture across facilities. The study sample was limited to HBO treatments administered in outpatient care facilities, where critical care patients are infrequently treated. Thus, adverse events associated with critical care hyperbaric therapy are likely underrepresented in the current sample.

**CONCLUSIONS**

Overall, the authors found that adverse event occurrence during HBO therapy is relatively infrequent and typically constitutes a low medical risk to the patient. When appropriate medical protocols are followed, the risk of an event is minimal. With effective patient education and precautionary pretreatment measures, some of the more frequently occurring events, such as confinement anxiety and hypoglycemia, could be further reduced. ●

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