

A Portuguese Case Study About Barotrauma

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Abstract. This work aimed to (Fijen 2016) determine the incidence and severity of barotrauma and identify the possibility of middle ear barotrauma in a high number of patients undergoing regular hyperbaric oxygen therapy. To explore and clarify this issue in terms of incident, seriousness and recurrence, age, gender, clinical signs, the specific history of chronic rhinitis, and symptoms of nasal obstruction during the occurrence were registered.

A first approach was performed by the authors where a descriptive statistical analysis and some elementary and intermediate statistical techniques such as variance analysis were performed. In the actual manuscript, a Logit model is built allowing us to relate the occurrence of barotrauma with the clinical profile of patients. We could conclude that Hyperbaric Oxygen Therapy is safe.

Keywords: Hyperbaric Oxygen Therapy · Logit Approach · Barotraumatism Occurrence · Middle Ear · Risk Factors

1 Introduction

Hyperbaric Oxygen Therapy (HBOT) is a treatment in which 100% oxygen (O2) is administered periodically in a chamber at a pressure above sea level. This growing intensity of O2 flow in the tissues allows the improvement of the treatment of ischemia and infection by reducing edema and tissue hypoxia (Acott 1999), (Mathieu 2006). Middle ear barotrauma (BTOM) is the most common complication. However, the incidence, risk factors, and severity are not fully understood. This work began with the collection of clinical characteristics of 1732 patients treated at the Portuguese Navy's Underwater and Hyperbaric Medicine Center (HMCS) from 2012 to 2016 presented in (Teles 2017), (M. F. Teodoro 2018), and (M. F. Teodoro 2018a). The socio-demographic details, frequency, severity, and recurrence were registered. This work focused in identify possible risk factors such as age, gender, clinical indications for HBOT, and history of allergic rhinitis. A statistical model was constructed to analyze the effect of gender and personal history of early-stage nasal obstruction on the probability of BTOM.

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Some risk factors are also identified in this section. Generalized least squares (GLM) methods (Nelder 1972), (Turkman 2000) were used to estimate the model. Some results are discussed in the present manuscript.

The structure of the work consists of 6 sections. Section 2 describes some of the adopted methods. Section 3 explains the principles of data collection. In Sect. 4, we recruited groups of 142 and 150 patients (without BTOM) from hyperbaric therapy patients using the study group (with BTOM) and control statistical methods. The first part uses basic techniques. An approximate model is also presented in Sect. 4. In the last section, we will discuss and reach some conclusions.

2 Preliminaries

2.1 HBOT

Hyperbaric oxygen therapy is a treatment used to accelerate recovery from carbon monoxide poisoning, gangrene, wounds that do not heal, and infections that require oxygen. For this treatment, we enter a special chamber to breathe pure oxygen at air pressure levels of 1.5 to 3 times above the media. The objective is to fill the blood with sufficient oxygen to repair the tissues and restore the body's normal function. HBOT helps wound healing by bringing oxygen-rich plasma to oxygen-depleted tissues (Hyperoxia). The sores cause damage to the body's blood vessels, which release fluid that leaks into the tissues and causes swelling. This swelling deprives the damaged cells of oxygen, and the tissue begins to die. HBOT reduces swelling while oxygenating tissues. More pressure in the chamber increases the amount of oxygen in the blood (Hyperoxemia). The goal of HBOT is to break the cycle of swelling, lack of oxygen, and tissue death. HBOT prevents "reperfusion injury". This is serious tissue damage that occurs when the blood returns to tissues after they have been deprived. For example, when blood flow is disrupted due to a crush injury, a series of events within damaged cells release harmful oxygen radicals. These molecules can cause irreversible tissue damage. They cause blood vessels to close and blood flow to stop. HBOT encourages the body's oxygen radical scavengers to seek out the problem molecules and allow healing to continue. HBOT helps to inhibit the action of harmful bacteria and strengthens the body's immune system. HBOT can inactivate toxins from certain bacteria. It also increases the concentration of oxygen in the tissues. This helps them to resist infection. In addition, this treatment improves the ability of white blood cells to find and destroy invaders. HBOT stimulates the formation of new collagen and new skin cells. It does this by stimulating the growth of new blood vessels. It also stimulates cells to produce certain substances, such as vascular endothelial growth factors. These attract and stimulate the endothelial cells needed for healing.

2.2 General Linear Models

In the classical linear model, a vector X with p explanatory variables $X = (X_1, X_{2,\ldots,} X_p)$ can explain the variability of the variable of interest Y (response variable), where $Y = Z\beta + \varepsilon$, where Z is some specification matrix, β a parameter vector and ε a random vector of errors.

The data are in the form (y_i, x_i), $i = 1,\ldots, n$, as a result of observation of (Y, X) n times. The response variable Y has an expected value $E[Y|Z] = \mu$.

Generalized linear models (GLM) formulation is an extension of the classical model where the response variable, follows an exponential family distribution (Turkman 2000) where the structure of the error does not need to have Gaussian distribution. Another extension from the classical model is that the function which relates the expected value and the explanatory variables can be any differentiable function b. Y_i has expected value

$$E[Y_i \backslash x_i] = \mu_i = b'(\theta_i),\ i = 1, \cdots, n.$$

It is also defined as a differentiable and monotone link function g which relates the random component with the systematic component of the response variable. The expected value μ_i is related to the linear predictor using the relation

$$\mu_i = h(\eta_i) = h(z_i^T \beta_i),\ \eta_i = g(\mu_i) \tag{1}$$

where h is a differentiable function and $g = h^{-1}$ is the link function; β is a vector of parameters with size p (the same size of the number of explanatory variables); z is a specification vector with size $p + 1$. A more detailed description of GLM can be found in (Turkman 2000). There are different link functions in GLM. When the random component of the response variable has a Poisson distribution, the link function is *logarithmic*, and the model is *log-linear*. Sometimes, the link function is unknown being estimated simultaneously with the linear component of the semi-parametric models. A detailed description of GLM methodology can be found in several references such as (Nelder 1972), (Turkman 2000).

3 Empirical Application

3.1 Sample

This study is a collaboration between the Medical Faculty of the University of Lisbon and the Center for Underwater and Hyperbaric Medicine of the Portuguese Navy. This study was a retrospective observational study designed in patients receiving routine hyperbaric oxygen therapy from January 1, 2012 to December 31, 2016.

All patients had an otolaryngologic (ORL) evaluation and tympanic examination prior to initiation of treatment. HBOT-trained volunteers who learned how to use Valsalva and Toynbee. Alerts you to warning signs and symptoms of complications. Only one patient with a type A tympanogram of the Jerger system was performed. (Audiologyonline 2023), (Jerger 1970), (Feldman 1976).

All tympanograms with maximum intratympanic pressure between −99 daPa and + 99 daPa and type A tympanograms according to Jerger's classification were considered "normal" (see Figures 1 and 2), the remaining tympanograms were "abnormal". An HBOT specialist nurse is always on hand to help patients with balance issues (equalizing difficulty).

If the patient reported otologic symptoms, the incident was recorded in the nurse's log, and the patient again underwent to perform a tympanogram and an otolaryngologic evaluation.

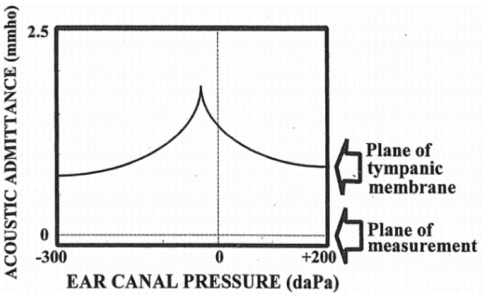

Fig. 1. A normal tympanogram. Peak with a small displacement from atmospheric pressure. Plan of measurement and plane of tympanic membrane. Adapted from (Feldman 1976).

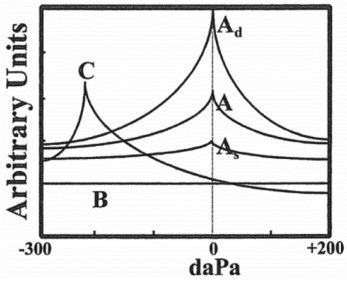

Fig. 2. Jerger classification illustration. Type A: peak near atmosphere pressure; Type Ad: high peak; Type As: smaller peak, Type B: flat; Type C: negative pressure. Adapted from (Feldman 1976).

The patients were included in a therapeutic protocol consisting of daily HBOT sessions, each session lasting 100 min, during which the patient was exposed to a pressure of 2.5 ata. The session begins with a 10-min compression phase followed by a 75-min treatment phase and a 15-min decompression phase. The treatment phase is divided into two consecutive 35-min breaks with 5-min breaks where the patient breathes air. During the compression and decompression phase, the patient breathes air.

Clinical records of all patients with symptoms consistent with BTOM (hearing discomfort, otalgia, numbness of the cephalic pinna, hearing loss, tinnitus and otorrhagia) were analyzed and clinical data were recorded: age, gender and clinical indications for HBOT (sudden deafness, sonotrauma, otitis externa, diabetic ischemia, chronic arterial disease, mandibular osteoradionecrosis, etc.). Symptoms of acute nasal obstruction at the time of onset may block the lumen of the tube and lead to tubal dysfunction (Fijen 2016).

An individual's medical history, including a previous diagnosis of allergic rhinitis and several commonly used medications associated with an increased risk of drug-induced non-allergic rhinitis, is considered at risk for chronic non-obstruction. For BTOM, location (right, left, or both ears), extent of lesion, frequency of recurrence, and post-BTOM middle ear pressure (high post-BTOM) were analyzed. A group of *150* patients were

randomly selected in the control population who did not experience BTOM during treatment. Statistical analysis was performed to compare clinical characteristics and confirm risk factors between the two groups. BTOM levels can be determined using a modified Teed classification (Teed 1944), first proposed by Wallace Teed (US Diver in World War II) and modified by Haines and Harris (Haines 1946). On a 6-step scale from 0° to 5°, the levels are shown in Table 1 and shown in the Fig. 3.

Table 1. Modified Teed classification: gravity of BTOM.

Modified Teed classification[a]	
Scale Level	Description
0	Symptomatology without otological signs
1	Diffuse hyperemia and tympanic membrane retention
2	Light hemorrhage within the tympanic membrane
3	Significant hemorrhage within the tympanic membrane
4	Outstanding and dark tympanic membrane
5	Free haemorrhage in the middle ear, with tympanic perforation, bleeding visible inside or outside the external auditory canal

a. A simpler description of the scale classification can be found in (), (Davis 2011).

3.2 Sample Characterization

To classify the data, firstly a study and control groups of *142* and *150* subjects were selected, respectively. In the first step, were calculated some simple measures using descriptive statistical techniques, and run some intermediate-level techniques (eg, tests of proportions, tests of independence, tests of comparison, others) (Tamhane 2000).

Given the non-quantitative nature of the relevant variables in the initial analysis of the data, measures of association, non-parametric Spearman correlation coefficients and non-parametric Friedman paired-sample tests were calculated. Figure 3 displays the classification of age in classes for the control and study groups. Age of the selected group of *178* patients who received HBOT. Control patients did not suffer from BTOM and all patients in the study group had BTOM during the treatment session. The minimum age of the control and study groups was *10* years, the maximum age was *83* years and the mean age was *55.05* and *55.36* years respectively. There was no evidence of differences between age distributions ($p\text{-}value = 0.80$). The study group consisted of *70* men and *72* women, and the control group consisted of 94 men and *56* women. Distribution by gender and group differed statistically ($p\text{-}value = 0.025$).

There exist several reasons that conduce to clinical indication for hyperbaric oxygen therapy. The diseases that implied the HBOT indication versus number of occurrences are shown in Fig. 4.

The most common clinical signs in the two groups were sudden deafness (*45%* and *57%* in the study and control groups, respectively), *radicular complications* (*31.47%* and

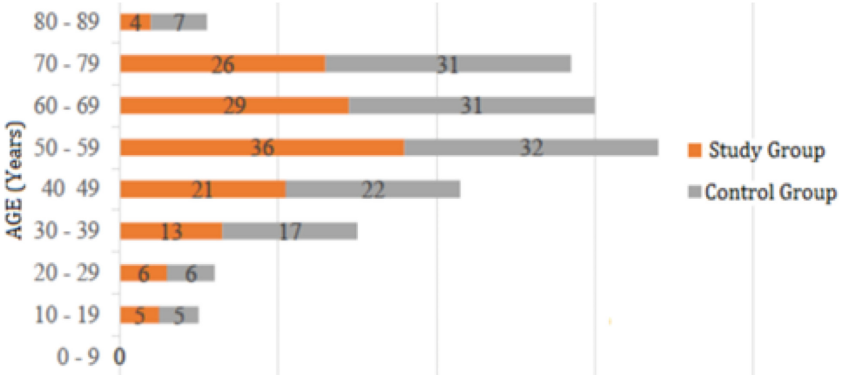

Fig. 3. Classification of age relatively to Control group e and Study group.

18%, respectively) and *diabetic ischaemia* (*10%* in each group)). Of the *radiographic problems*, *radicular cystitis* was the most common in both groups (*13.2%* and *11%*). *Osteonecrosis of the lower jaw* in the study group (9.8%) and the control group (*2%*) were distinct. The prevalence of *rheumatoid arthritis* in each group was similar (approximately *4%* in each group).

Evaluating *sudden deafness* (more in the control group, $p = 0.025$) and *osteonecrosis of the jaw* (more in the study group, $p = 0.028$) were statistically significant between the two groups. The difference in the rates of diagnoses of *rickettsial cystitis* and *radial proctitis* between the two groups was not statistically significant.

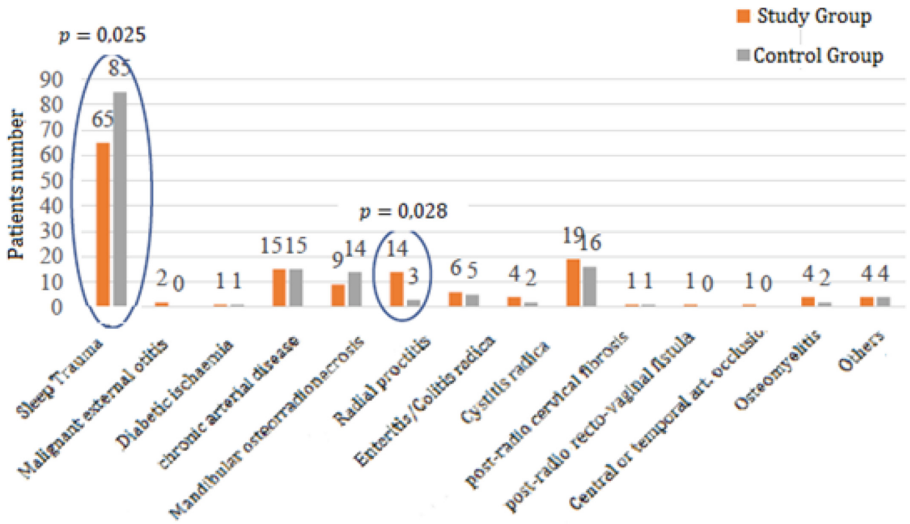

Fig. 4. Number of patients per disease with HBOT prescription.

The characteristics of BTOM in patients are shown in Table 2. Table 2 considers the frequency and number of treatment sessions until BTOM develops. Between 1732 patients, 143 had BTOM, and the incidence of patients with BTOM was approximately 8.3%. Only 41% of patients had complete information recorded during the clinical process. From the data collected (see Table 2), BTOM occurred in 36% of cases in the first 3 sessions (19% in the first session) and in 44% of cases up to 5 sessions. The incidence of BTOM in patients was 8.3%, with the majority of cases being unilateral in 62% and the remaining 21% cases being bilateral. The recurrence rate was 28%.

Among patients with middle ear injuries, most patients (62%) had unilateral BTOM (mostly in the right ear). A significant proportion (21%) suffered BTOM in both ears during the same session. The results obtained were 34% BTOM in the right ear, 28% in the left ear and 21% in both ears. As shown in Table 3 and Fig. 5, the BTOM gravity, considering the number of unilateral and bilateral recurrent BTOMs, totals 208 BTOMs per ear.

Most were rated with level 1 of Teed classification (30%). Approximately 20% of analyzed ears scored 3 or higher in this classification. The number of BTOM ears (reference) in each category are shown in Table 3. About 50% of BTOM ears are classified in the first four levels, and almost 20% of BTOM ears are more severe (classified as 4 or 5). In 57 cases (27%), BTOM was not documented in the process (physician not registered or patient did not choose to see a specialist other than his own specialist out of CMSH) and could not be classified.

Table 2. Number of sessions at the time of BTOM occurrence per number of patients.

Number of sessions	Number of patients
0–3	21
4–5	25
6–9	9
10–14	5
15–19	3
20–99	6
29–49	3
50–69	5
70–99	1
>100	1

Table 3. Percentage of BTOM ears per gravity level (considering modified Teed classification).

BTOM gravity Modified Teed classification	
Scale Level	Percentage of BTOM ears
0	5.77
1	30.00
2	17.00
3	9.13
4	9.61
5	1.44

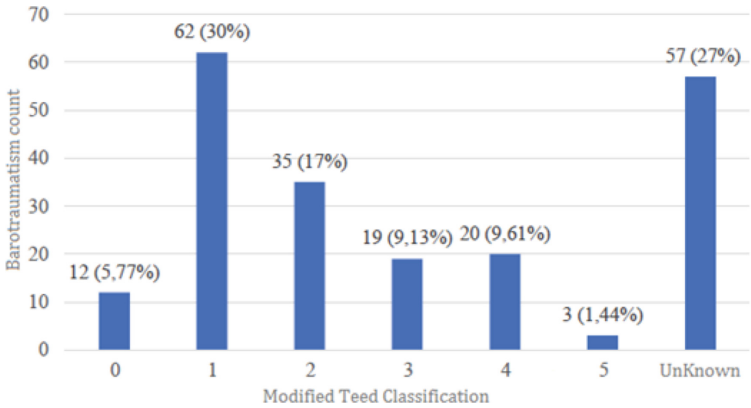

Fig. 5. Gravity of BTOM. Teed modified classification.

4 The Model

In this section are presented some models after the process of estimation by GLM, validation and selection of the models, and testing some distinct link functions g to estimate adequate models. The *log-log*, *logistic,* and *probit* regression were taken into consideration. To get the "'best" explanatory variables in each case, was used the stepwise selection.

Once we have dichotomous data, discrete models were preferably estimated by logistic and probit regression. Almost all estimated and selected models have validation tests with *p-values* between 0.001 and 0.08. In the estimation process, we did not take into consideration some potential variables due the fact that the patient's medical register had a lot of miss information. The residential area and race, once there were few individuals had a complete register. The description and codification of considered variables are in Table 4.

The logistic model relative to the dependent variable Y1, was obtained in several steps. Initially, the selection of the best set of covariates that conduces to the "best"

model, was done by stepwise, based on the p-values from Wilks test likelihood ratio relative to inclusion/exclusion of covariates. The impact of a covariate in the occurrence of barotraumatism is measured by the obtained *p-value*: a small *p-value* means a significant influence. First are selected the principal effects, and last, the second-order interaction. Female gender, diagnosis of osteoradionecrosis of the mandible, and personal history of allergic rhinitis were identified (statistically significant) as risk factors. No significant relationships were found between age, remaining clinical indications, risk medication, and changes in tympanogram performed prior to initiation of treatment when we consider models without interaction. When the models are estimated with interaction, we have significance with gender, allergic rhinitis, and corticoid therapeutic, another significant interaction was obtained with number of sessions and osteoradionecrosis when we consider the barotrauma classification as dependent variable.

Table 4. Codification of considered variables.

Variables	Description	Codification
Y_1	BTOM occurence	1 = Yes 0 = No
Y_2	Teed Classification level	0 = (0, 1, 2) low 1 = (3, 4, 5) high
Y_3	Type of BTOM	0 = no occurrence 1 = unilateral 2 = bilateral
X_1	Number of sessions	1, ….9 = 1…..9 10 = greater than 9
X_2	diagnosis of osteoradionecrosis	1 = Yes 0 = No
X_3	history of allergic rhinitis	1 = Yes 0 = No
X_4	Cortcoid therapeutic	1 = Yes 0 = No
X_5	tympanogram	1 = Yes 0 = No
X_6	age	‘1’ = (<18) ‘2’ = ([18. 29]) ‘3’ = ([30.49]) ‘4’ = (≥50)
X_7	Gender	0 = Female 1 = Male

Relatively to BTOM occurrence (the aim of study), the obtained model considering principal effects (gender, allergic rhinitis, diagnosis of osteoradionecrosis) is given by structural form (2). We also found some significant interactions between the diagnosis of

osteoradionecrosis and allergic rhinitis in females. The estimated model for barotrauma classification (high/low) as the dependent variable, considering principal and second and third-order effects, is summarized in structural Eq. (3).

$$\ln\left[\frac{\pi_i}{1-\pi_i}\right] = \beta_0 + \sum_{j=1}^{3} \beta_j x_{ij} \tag{2}$$

$$\ln\left[\frac{\pi_i}{1-\pi_i}\right] = \alpha_0 + \sum_{j=1}^{2} \alpha_j x_{ij} + \alpha_3 x_{i1} x_{i2} + \alpha_4 x_{i7} x_{i3} x_{i4} \tag{3}$$

The significant explanatory variables and parameters p-value of models (2) and (3) are displayed in Table 5 and include some significant interactions. Model (2) has a deviance global test with *p-value = 0,010*, by other hand, model (3) conduces to *p-value = 0.015*. Another evaluation of models is done by residual analysis.

When all validation and selection techniques are completed, we need to be able to choose correctly between different models with close explanatory performance. The best models with similar performance conduce to estimates which are combined using a weighted mean using the p-values of the global test.

Table 5. Models parameters. Model (2) without interaction; Model (3) with interaction.

Effect	Parameter Model (2)	P-value Model (2)	Parameter Model (3)	P-value Model (3)
Intercept	$\hat{\beta}_0$	0.001	$\hat{\alpha}_0$	0.002
(x_2)	$\hat{\beta}_1$	0.004	$\hat{\alpha}_1$	0.005
(x_3)	$\hat{\beta}_2$	0.005		
(x_7)	$\hat{\beta}_3$	0.004		
$(x_7.x_2.x_3)$	$\hat{\beta}_4$	0.05	$\hat{\alpha}_3$	0.004
$(x_1.x_2)$			$\hat{\alpha}_4$	0.06
$(x_7.x_3.x_4)$			$\hat{\alpha}_4$	0.004

We are interested in the comparison of odd ratios for different values of explanatory variables. The odd ratios for the two identified models A (without and with interactions) and B (with interactions) are given by formulae (4) and (5) respectively.

$$\Psi = \left[\frac{\pi_i}{1-\pi_i}\right] = \exp\left[\beta_0 + \sum_{j=1}^{3} \beta_j x_{ij}\right] \tag{4}$$

$$\Psi = \left[\frac{\pi_i}{1-\pi_i}\right] = \exp\left[\alpha_0 + \sum_{j=1}^{2} \alpha_j x_{ij} + \alpha_3 x_{i1} x_{i2} + \alpha_4 x_{i7} x_{i3} x_{i4}\right] \tag{5}$$

5 Discussion

The evaluation about the possibility of occurrence of BTOM and the establishment of some association with some the individual characteristics/clinical profile of patients can be done. From formulae (4) and (5) we can estimate the odds ratio for some values of explanatory variables. For example, the odd ratio (Higher/Lower) for two females with historical allergic rhinitis with and without therapeutic, the value of the odd ratio is lower than one, supposing that they have similar remaining characteristics. It means that the probability of a higher Teed classification is less than the probability of a lower Teed classification (using model (5)).

Using the model (4) for the same gender, considering two patients with allergic rhinitis, we have the odd ratio greater than one, if only one of both patients has osteoradionecrosis and considering the same values of remaining explanatory variables. This means that the probability of BTOM increases relatively to a patient with osteoradionecrosis comparatively with another patient without osteoradionecrosis. Other relations and a detailed analysis can be performed in detail and it is planned for the future.

6 Conclusion

HBOT is an effective and safe medical therapy. Proper teaching of the active leveling maneuver and careful monitoring during the first session can significantly reduce the incidence of BTOM. The CMSH of the Portuguese Navy has 8:3% BTOM, mainly in low gravity. The risk of recurrence needs to be assessed, consequently some patients need to take prophylactic medication during the treatment period. The aim of the study was to determine the incidence and severity, also to detect risk factors for middle ear barotrauma in a population of patients attending hyperbaric oxygen therapy.

Several general linear models were computed allowing to get a set of explanatory variables, some of them were identified as risk variables. In a model without interaction, male gender, diagnosis of osteoradionecrosis of the jaw, and history of allergic rhinitis were statistically significant. There was no significant relationship between age, other clinical indications, treatment risk and tympanogram changes made before HBOT.

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