Original research article

The predictive value of transcutaneous oxygen tension measurement in diabetic lower extremity ulcers treated with hyperbaric oxygen therapy: a retrospective analysis of 1144 patients

CAROLINE E. FIFE, MD[a]; CEM BUYUKCAKIR, MD[b]; GORDON H. OTTO, PhD[c]; PAUL J. SHEFFIELD, PhD[d]; ROBERT A. WARRINER III, MD[e]; TOMMY L. LOVE, DO[f]; JON MADER, MD[g]

The objective of this retrospective analysis was to determine the reliability of transcutaneous oxygen tension measurement ($TcPO_2$) in predicting outcomes of diabetics who underwent hyperbaric oxygen therapy for lower extremity wounds. Six hyperbaric facilities provided $TcPO_2$ data under several possible conditions: breathing air, breathing oxygen at sea level, and breathing oxygen in the chamber. Overall, 75.6% of the patients improved after hyperbaric oxygen therapy. Baseline sea-level air $TcPO_2$ identified the degree of tissue hypoxia but had little statistical relationship with outcome prediction because some patients healed after hyperbaric oxygen therapy despite very low prehyperbaric $TcPO_2$ values. Breathing oxygen at sea level was unreliable for predicting failure, but 68% reliable for predicting success after hyperbaric oxygen therapy. $TcPO_2$ measured in chamber provides the best single discriminator between success and failure of hyperbaric oxygen therapy using a cutoff score of 200 mmHg. The reliability of in-chamber $TcPO_2$ as an isolated measure was 74% with a positive predictive value of 58%. Better results can be obtained by combining information about sea-level air and in-chamber oxygen. A sea-level air $TcPO_2$ < 15 mmHg combined with an in-chamber $TcPO_2$ < 400 mmHg predicts failure of hyperbaric oxygen therapy with a reliability of 75.8% and a positive predictive value of 73.3%. **(WOUND REP REG 2002;10:198–207)**

From the Department of Anesthesiology[a], The University of Texas Medical School at Houston, and the Memorial Hermann Center for Hyperbaric Medicine, Houston, Texas; GMMA Aerospace Medical Center[b], Eskisohir, Turkey; Belk College of Business[c], The University of North Carolina at Charlotte, Charlotte, North Carolina; Nix Wound Care and Hyperbaric Medicine Facility[d], Nix Medical Center, San Antonio, Texas; Southeast Texas Center for Wound Care and Hyperbaric Medicine[e], Conroe, Texas; Utah Center for Wound Healing and Hyperbaric Medicine[f], Bountiful, Utah; and Department of Internal Medicine[g], The University of Texas Medical Branch, Galveston, Texas.

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Reprint requests: Caroline E. Fife, MD, 6431 Fannin, MSB 5.020, Houston, TX 77030. Fax: (713) 704-5793; E-mail: Caroline.E.Fife@uth.tmc.edu.

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ATA	Atmosphere absolute
HBO_2T	Hyperbaric oxygen therapy
PPV	Positive predictive value
$TcPO_2$	Transcutaneous oxygen tension

Hyperbaric oxygen therapy (HBO_2T) is the inhalation of 100% oxygen by a patient enclosed in a pressure vessel or chamber. For wound healing, hyperbaric chambers are usually pressurized to simulate an atmospheric pressure 2–2.5 times sea level. The dramatic increase in plasma-dissolved oxygen achieved during HBO_2T can supply tissues with adequate oxygen to support metabolism, even if the vascular supply is compromised.[1] As a result, HBO_2T has been used as adjunctive therapy for certain types of hypoxic wounds including compromised skin grafts and diabetic lower extremity wounds. Randomized, controlled trials have shown the benefit of HBO_2T in diabetic ulcers of the lower extremity.[2–7] The economic and emotional costs of amputation and rehabilitation easily exceed the cost of

HBO_2T when successful.[8] A reliable method of wound assessment that excludes patients likely to fail enhances cost-effectiveness. Transcutaneous oximetry has gained importance as a tool for selecting HBO_2T candidates.[9] The objective of our analysis was to determine the accuracy and predictive value of transcutaneous oxygen tension ($TcPO_2$) in predicting the likelihood of benefit or failure of HBO_2T, using data from a very large series of patients.

The technique of $TcPO_2$ measurement has been well described[9] and previously shown in small studies to be useful in selecting patients who are unlikely to heal spontaneously.[10–12] It has also been shown to be helpful in predicting which patients are likely to benefit from HBO_2T,[13] but small sample sizes have limited the ability to assess the accuracy and reliability of $TcPO_2$. A variety of techniques have been employed to enhance the predictive value of $TcPO_2$. Observing the absolute value and the relative increase in $TcPO_2$ while breathing oxygen at sea level seems to increase the accuracy of $TcPO_2$ in post-amputation healing.[14–16] It has also been shown to be of benefit in predicting outcome from hyperbaric oxygen therapy,[14–16] although the accuracy of this approach has not been evaluated. In-chamber $TcPO_2$ has previously been shown to have the strongest statistical relationship to benefit from HBO_2T.[13] However, until now the number of observations in each of these studies was inadequate to assign accuracy. Although the data in this study were retrospectively obtained, this is the largest analysis of its kind.

MATERIALS AND METHODS

One physician reviewed 1006 records of patients with diabetes from five Texas hyperbaric medical facilities. Records from an additional 79 patients at Travis Air Force Base in California and 59 patients from Memorial Hermann Hospital in Texas were reviewed by a different examiner. These 1144 records comprised all diabetic patients treated at each facility since its inception, and therefore spanned a time frame of approximately 10 years at the oldest facility. All charts were examined for details of medical history, treatment, outcome, and available follow-up. Permission for the study was obtained from the Committee for the Protection of Human Subjects at The University of Texas Health Science Center (Houston) and from other participating units (Appendix).

Wound assessment and outcome characterization

The severity of each lower extremity wound was assessed using a modified Wagner grading scale[17] as follows: Grade I, superficial ulcer; Grade II, deep ulcer to tendon, capsule, or bone; Grade III, deep ulcer with abscess, osteomyelitis, or joint sepsis; Grade IV, localized gangrene of forefoot or heel; and Grade V, gangrene of the entire foot. If a Wagner grade was not designated in the record, the reviewer determined the grade by studying the description of the wound and photographs taken at the time of initial evaluation. Photographs were available on all patients. Racial and ethnic groups were described as black, white, Hispanic or Oriental. Approximately 22% of patients had more than one wound at the initiation of HBO_2T. The physician observer recorded the number of lesions, and the lesion with the highest modified Wagner score was selected for study. Outcome at the completion of HBO_2T was determined by assigning the study wound to one of five categories: 1) healed (complete epithelialization); 2) partially healed (granulating); 3) no apparent healing; 4) amputated; or 5) died before treatment was completed. It is important to note that if the description or photograph of the wound did not show complete epthelialization, even if the wound was completely granulated, the wound was designated as "partially healed." Thus the category of "partially healed" represents a broad category of wounds with varying degrees of granulation. Wounds showing either complete healing (complete epithelialization) or partial or complete granulation were felt to have achieved benefit from hyperbaric therapy. Wounds that showed no apparent healing (no granulation) or limbs that were amputated were designated as "failed." Because patients usually undergo HBO_2T at least 5 days a week, an interruption in treatment was arbitrarily defined as receiving three or fewer treatments per week for two or more weeks or missing five consecutive treatments. The classification of outcome at follow-up was: 1) healed (complete epithelialization); 2) draining; 3) amputated; and 4) died. In this retrospective study, it was not possible to standardize wound treatment. However, the contributing hyperbaric facilities were experienced wound care centers, and the principles of moist wound dressings were considered standard care. Follow-up information was obtained from the verbal descriptions in the chart and photographic documentation. Because this was a retrospective study, the availability of follow-up information was highly variable.

$TcPO_2$ measurements

Transcutaneous oxygen measurements were obtained with either Radiometer or Novametrics devices, set at a temperature of 44 °C.[18] The reviewer looked at the photograph of the wound location and then determined which of the leads was closest to the wound. Multiple $TcPO_2$ values were available in all patients. We chose the smallest numeric value of the leads in the "peri-wound" area, regardless of whether it was proximal or distal to the wound. Transcutaneous oxygen values were recorded under three possible conditions, although not all data were available in all patients: 1) breathing air at sea level; 2) breathing oxygen at sea level; and 3) breathing oxygen in the hyperbaric chamber. When sea-level oxygen challenge data were available, the analysis included the absolute value of sea-level oxygen $TcPO_2$, the absolute increase in mmHg over the sea-level air $TcPO_2$, and the percent increase compared with the air $TcPO_2$. Because in-chamber $TcPO_2$ is a relatively recent development, not all patients underwent in-chamber $TcPO_2$ testing.

Statistical analysis

The data were initially recorded by the chart reviewer on an Excel spreadsheet. These were then compiled into an SPSS database for statistical analysis. With the exception of the model presented in Figure 2, all statistical analyses were conducted using contingency tables in which Pearson's chi-square analysis was employed to compute the p-values reported (without the Yates correction factor). When tables were constructed to compare two or more groups ("renal failure" vs. "standard care") the Mantel-Haenszel procedure was employed. Multivariate tabulations employing different $TcPO_2$ measurements were developed as part of the analytical process. These included combinations of factors such as baseline air $TcPO_2$ in conjunction with in-chamber $TcPO_2$, originally described by Myers and Emhoff,[19] and the effects of Wagner score on the predictive value of $TcPO_2$.

We employed the following definitions with respect to using $TcPO_2$ cutoff scores to identify candidates for treatment failure. Failure is defined as those with amputation or no healing. Success is defined as those with at least some healing at the termination of HBO_2T. Other definitions: 1) positive predictive value (PPV) is the percent of patients predicted to fail who actually failed; 2) false-negative rate is the percent of patients predicted to heal who actually failed; 3) sensitivity is the percent of patients who will fail and who are correctly identified as failures by the cutoff score; 4) specificity is the percent of the group who will heal that are predicted to heal; 5) reliability (accuracy) is the percent of overall correct assessments.

RESULTS

Records of 1144 diabetic patients were reviewed. The outcomes of 68 patients were not obtainable, and nine patients died during treatment. This left 1067 subjects whose outcomes could be analyzed. Overall, 75.6% of the patients were noted to have an improvement in the wound following HBO_2T. Patients who improved after HBO_2T received a mean of 34 treatments, while those who did not improve received a mean of 24 treatments, apparently because HBO_2T was discontinued if the patient did not appear to be improving. In 77% of improved patients, HBO_2T was discontinued when the wound was granulated rather than continuing to complete epithelialization. Wound severity, as measured by the modified Wagner score, was the single most important determinant of whether patients improved after a course of HBO_2T ($p < 0.001$). Modified Wagner Grades IV and V wounds had success rates of only 64.5% and 29.7%, respectively. Women were 42% of the total study population and there were no differences in outcome between men and women ($p = 0.28$). Treatment outcome was not significantly different between the racial groups ($p = 0.40$). Hispanics comprised 43.9% of the population because of the prevalence of this ethnic group in Texas and California.

Overall, only 60.4% of the renal failure patients were helped by HBO_2T compared with 71.7% of the nonrenal failure patients. The pattern of poorer response was continued when the patients were compared by Wagner score ($p < 0.001$), with Wagner scores III and IV defining 79% of the patients in each group. For this reason it was determined that renal failure patients should be viewed as a medically separate population and removed from the data in this study. Removing this subset did not impact the data analysis because of the small number of renal failure patients in comparison with the total. In a similar fashion, the 194 patients receiving a topical platelet-derived growth factor preparation (Procuren®) were determined to have been treated differently from "standard care" patients. Patients receiving Procuren® had a statistically greater number of hyperbaric oxygen treatments for any given outcome and had higher baseline transcutaneous values than the other patients. They were removed as well, leaving 774 standard care patients as the database to be analyzed in this paper.

One hundred eighteen (15.27%) patients were classified as having an interrupted treatment regimen. The interrupted group had a success rate of 62.7% compared with 75.7% in the noninterrupted group. This was statistically significant ($p = 0.003$). In addition, while both groups averaged almost the same $TcPO_2$ in air and in sea-level oxygen, the interrupted group averaged nine more HBO_2Ts than the noninterrupted group, suggesting that an interruption in treatment regimen resulted in more total treatments being needed for the same outcome.

Table 1 shows the relationship between outcome at the time HBO_2T was discontinued and subsequent follow-up assessment for all patients in whom follow-up information was available (756 of 1144). In general, wounds that were classified as "healed" at the conclusion of HBO_2T were still healed at follow-up (median time of 2 weeks). Of those patients whose wounds were "partially healed" at

Table 1. Outcome at termination of hyperbaric treatment versus follow-up assessment of the worst lesion

	Outcome class at termination of HBO_2T				
Wound status at follow-up	**Healed (%)**	**Partial healing (%)**	**No healing (%)**	**Amputation (%)**	**Totals (%)**
Healed	99.2	87.4	5.3	5.2	68.4 (517)
Draining	0.0	8.1	50.0	3.9	8.1 (61)
Amputation	0.8	3.4	34.2	85.1	21.2 (160)
Died	0.0	1.1	10.5	5.8	2.4 (18)
Combined total	100.0 (118)	100.0 (446)	100.0 (38)	100.0 (154)	100.0 (756)
Time elapsed from termination of HBO_2T to follow-up (wks)					
Median	2	4	4	2	
75th percentile	8	15	8	3.5	

n = 756 patients.

Table 2. Sea-level $TcPO_2$ in air as a screening tool for failure of hyperbaric oxygen therapy

Cutoff score of screen (mmHg)	Positive predictive value (%)	False-positive rate (%)	False-negative rate (%)	Reliability (% correct)	Sensitivity (%)	Specificity (%)
Ideal	100	0	0	100	High	High
25	34.8	65.2	20.6	55.1	66.9	50.4
20	35.7	64.3	22.0	58.4	58.4	58.4
15	35.4	64.6	24.0	60.5	47.8	65.6
10	37.7	62.3	24.5	64.5	38.8	74.7
5	38.3	61.7	25.8	66.9	27.5	76.8
3	40.4	59.6	26.3	68.9	20.2	84.4
Treat all	n/a	n/a	28.3	71.7	n/a	n/a

n = 629 patients.

the end of a course of HBO_2T, 87% were noted to be healed (completely epithelialized) at follow-up (median time of 4 weeks). The majority of patients with no evidence of healing at the time hyperbaric oxygen therapy was discontinued either had a draining wound or had undergone an amputation at follow-up. In those patients who underwent an amputation at the end of their hyperbaric treatment, nearly 6% were subsequently noted to have died within the follow-up period. The categories of "healed" and "draining" wounds in the follow-up of the amputation group refer to the stump site. Unfortunately, the follow-up time had a median value of only 3 weeks, which is too soon after discharge to be a convincing predictor of outcome stability. However, even in this brief period, there was a high rate of death or amputation among those with no evidence of healing at the conclusion of hyperbaric therapy and a low rate of amputation among those who were helped by treatment.

There was no statistical difference between the 136 patients treated at 2.0 atmosphere absolute (ATA) and the 638 treated at 2.4 ATA ($p = 0.75$). However, because there was a significant statistical relationship between in-chamber $TcPO_2$ and outcome (to be discussed), it is possible that the critical value was the tissue oxygen level achieved during treatment, rather than the treatment pressure. In-chamber $TcPO_2$s were highly variable regardless of treatment pressure. In this retrospective study it was not possible to determine whether a higher treatment pressure resulted in higher in-chamber $TcPO_2$s.

$TcPO_2$ data

Sea-level air $TcPO_2$ data for the 629 patients are presented in Table 2. The purpose of the sea-level air $TcPO_2$ was to determine the degree of tissue hypoxia near the wound. Patients with an air value of ≥ 25 mmHg had a 2.5 times greater likelihood of benefiting from HBO_2T compared with those having a $TcPO_2 < 25$ mmHg ($p = 0.001$). However, when various potential cutoff scores were evaluated, the PPVs of these screens were all below 50%. For example, even taking a very low baseline value such as 15 mmHg as a cutoff (the value below which healing even with HBO_2T might not be expected) fewer than half the patients predicted to fail actually failed.

Sea-level $TcPO_2$ breathing oxygen data

Table 3 shows the absolute $TcPO_2$ value while breathing oxygen at sea-level, which was available for 499 patients. The purpose of the oxygen challenge was to assess whether the wounded area would respond to oxygen administration. It is apparent that all cutoff scores for values ≥ 25 mmHg while breathing oxygen performed better than any cutoff score on air, regardless of whether

Table 3. Absolute sea-level oxygen $TcPO_2$ as a screening tool for failure of hyperbaric oxygen therapy

Cutoff score of screen (mmHg)	Positive predictive value (%)	False-negative rate (%)	Reliability (% correct)	Sensitivity (%)	Specificity (%)
Ideal	100%	0%	100%	High	High
50	37.8	19.0	64.4	55.7	67.4
40	41.2	19.2	68.1	50.4	74.5
35	41.1	20.1	68.5	45.8	76.6
30	41.5	20.9	69.3	41.2	79.3
25	42.0	21.3	69.9	38.2	81.3
20	39.6	23.0	69.5	30.5	83.4
10	32.8	25.4	69.7	14.5	89.4

n = 499 patients.

Table 4. Percent increase in $TcPO_2$ after sea-level oxygen challenge in relation to failure of hyperbaric oxygen therapy

Percent increase	Percent Failed (n)
≤ 0	36.4 (33)
0.1–50%	29.4 (51)
50.1–100%	25.0 (64)
100.1–200%	31.5 (92)
200.1–300%	23.9 (71)
300.1–400%	23.8 (42)
400.1–500%	25.0 (36)
More than 500%	21.8 (110)
Overall	26.3 (499)

n = 499 patients.

PPV or reliability is used. Achieving $TcPO_2$ values of 25–30 mmHg while breathing sea-level oxygen had 69% reliability in predicting healing after hyperbaric oxygen therapy, with a 21% false-negative rate. Another approach to assessing $TcPO_2$ response to the oxygen challenge is to compare the percent or ratio of the reading while breathing oxygen to the reading in air (e.g., a 50% increase is a ratio of 1.5). Table 4 shows the failure rate and sample size in selected ranges of the percent increase in $TcPO_2$ during oxygen challenge. A decrease (or no increase) in $TcPO_2$ with sea-level oxygen breathing was the most predictive of failure. However, this criterion had a PPV of only 36.4%. The largest separation comes when the $TcPO_2$ in oxygen at least triples. Despite this, when the data are cast into a decision table with the cutoff score set at 200% (tripling), the reliability is only 54.2% and the false-negative rate is 70%. Thus, the percentage increase in $TcPO_2$ with oxygen breathing performs poorly as a predictor of healing with hyperbaric oxygen therapy.

An analysis of the absolute increase (in mmHg) with sea-level oxygen breathing is more encouraging. Table 5 summarizes these data.

An increase of either 15 or 20 mmHg with oxygen breathing provides equivalent reliability, and both of these values perform better than an increase of only 10 mmHg. When compared with Table 5, however, analyzing the increase in $TcPO_2$ from baseline is seen to perform no better than the absolute level of $TcPO_2$ in oxygen. Also, the absolute increase in mmHg with sea-level oxygen breathing (Table 5) is superior to evaluating a percentage increase. The distribution of the increase is shown in Figure 1. The data suggest that the absolute $TcPO_2$ value while breathing sea-level oxygen is the most useful of the various methods of analyzing sea-level $TcPO_2$ data. The test of sea-level oxygen breathing may approach a reliability of 70%. To improve reliability, more complex models are needed that incorporate additional indicators and/or functional relationships to strengthen their contributions.[20]

In-chamber $TcPO_2$ measurements

In-chamber $TcPO_2$ readings were taken on a subset of 221 patients. Table 6 reports the statistics associated with alternative cutoff scores. Of those with in-chamber $TcPO_2$ levels < 100 mmHg, only 10% of patients were better after HBO_2T. Of those with in-chamber $TcPO_2$ levels > 500 mmHg, 78.8% were improved after HBO_2T. While 150 mmHg has a higher PPV, it identifies only 18.3% of the failures, whereas 100 mmHg identifies too few total patients (4.5%). In this data set, a cutoff score of 200 mmHg may be the best choice because it identifies an "at-risk"

Table 5. Absolute increase in $TcPO_2$ with oxygen challenge as a screening tool for failure of hyperbaric oxygen therapy

Cutoff increase (mmHg)	Positive predictive value (%)	False-negative rate (%)	Reliability (% correct)	Sensitivity (%)	Specificity (%)
Ideal	100	0	100	High	High
20	40.1	20.2	67.5	47.7	74.3
15	41.5	20.9	68.9	42.4	78.4
10	37.8	23.3	68.1	31.8	81.1
5	38.5	24.3	69.9	22.7	86.9
0	31.4	25.9	69.7	12.1	90.4

n = 499 patients.

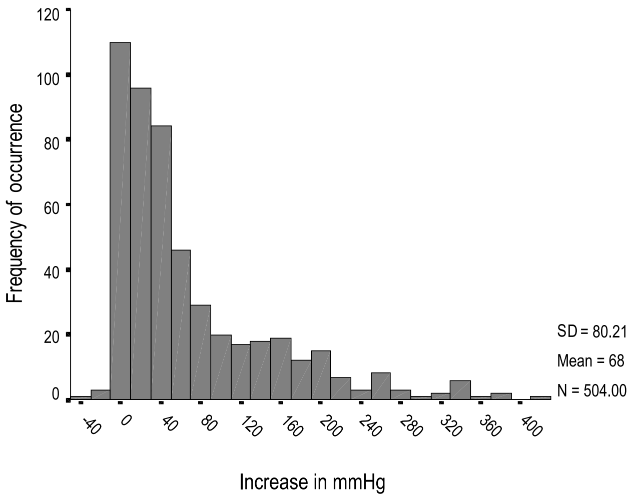

FIGURE 1. Distribution of $TcPO_2$ values during sea-level oxygen breathing.

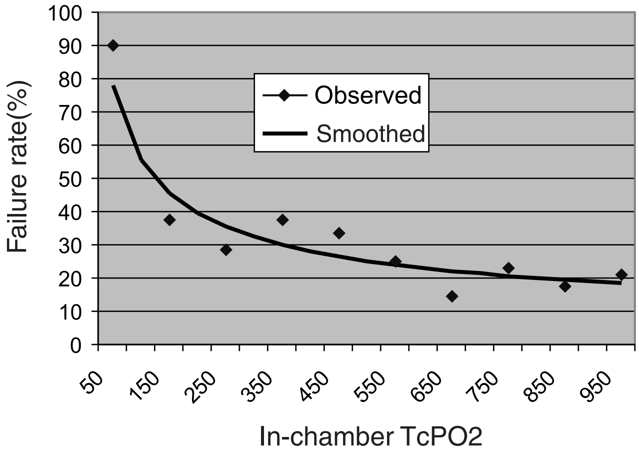

FIGURE 2. Estimate of the failure rate of HBO_2T in relation to in-chamber $TcPO_2$. Failure rate increases as in-chamber $TcPO_2$ decreases. However, as in-chamber $TcPO_2$ increases above 400 mmHg, there is little incremental improvement in healing likelihood.

group large enough to make screening worthwhile. If the in-chamber $TcPO_2$ is less than 200 mmHg, then the likelihood of failure is at least 58%. It appears that once some threshold value of in-chamber $TcPO_2$ is achieved, reaching even higher in-chamber values does not confer a significant improvement in outcome scores. Table 7 shows the failure rate associated with various ranges of in-chamber $TcPO_2$ values. This is different from the information in Table 6, which aggregates the data for all values below the cutoff score versus all values above the cutoff. The data in Table 7 are lumpy due to the small sample sizes in the low $TcPO_2$ ranges. A smooth curve through the data provides a better picture of the relationship between decreasing in-chamber $TcPO_2$ and treatment failure. The best smooth curve fitted through these data, using the midpoint of the interval as the point of concentration of the failure rate, is: Failure rate (%) $= 535.408\ (TcPO_2)^{-0.492}$; $R^2 = 0.76$, and the p-value $=$ 0.0005.

This equation is plotted in Figure 2 and allows one to estimate the failure rate as a function of the in-chamber $TcPO_2$ value.

Table 7. In-chamber $TcPO_2$ versus outcome

In-chamber $TcPO_2$(mmHg)	Failure rate (%)	No. of patients
< 100	90.0	10
100–199	35.7	14
200–299	28.6	7
300–399	35.7	14
400–499	33.3	18
500–599	29.4	17
600–699	14.3	14
700–799	23.1	26
800–899	17.4	23
900 and higher	20.5	78
Overall	27.3	221

n = 221 patients.

Myers and Emhoff–type analysis

Myers and Emhoff[19] studied a small set of diabetic patients ($n = 11$) and concluded that for estimating between success and failure, those patients whose $TcPO_2$ in air was < 20 mmHg would need an in-chamber

Table 6. In-chamber $TcPO_2$ versus outcome as a screening tool for failure of hyperbaric oxygen therapy

Cutoff score (mmHg)	Positive predictive value (%)	False-negative rate (%)	Reliability (% correct)	Sensitivity (%)	Specificity (%)
Ideal	100	0	100	High	High
600	39.5	20.1	65.0	53.3	69.8
500	42.2	21.2	68.2	45.0	76.9
450	43.4	22.2	69.5	38.3	81.3
400	46.7	22.3	71.4	35.0	85.0
300	51.6	23.3	73.2	26.7	90.6
250	55.6	23.3	74.1	25.0	92.5
200	58.3	23.5	74.5	23.3	93.8
150	61.1	24.3	74.5	18.3	95.6
100	90.0	24.3	76.4	15.0	99.4

n = 221 patients.

Table 8. Sea-level air $TcPO_2$ versus in-chamber $TcPO_2$ as a screening tool for failure of hyperbaric oxygen therapy

In air at sea-level	In-chamber < 500 mmHg	In-chamber < 400 mmHg	In-chamber < 300 mmHg
< 20 mmHg	PPV = 58.6% Reliability = 74.9% Sensitivity = 28.8% n = 29	PPV = 65.0% Reliability. = 75.3% Sensitivity = 18.6% n = 20	PPV = 64.3% Reliability. = 74.4% Sensitivity = 15.3% n = 14
< 15 mmHg	PPV = 68.2% Reliability. = 76.3% Sensitivity = 25.4% n = 22	PPV = 73.3% Reliability = 75.8% Sensitivity = 18.6% n = 15	PPV = 77.8% Reliability = 74.9% Sensitivity = 11.9% n = 9
< 10 mmHg	PPV = 66.7% Reliability. = 74.9% Sensitivity = 16.9% n = 15	PPV = 80.0% Reliability = 75.3% Sensitivity = 13.6% n = 10	PPV = 80.0% Reliability = 74.0% Sensitivity = 6.8% n = 5

Table 9. Modified Wagner score and outcome after HBO_2T

Wagner score	Sample size	Helped by HBO_2T (%)
I	3	100.0
II	130	83.1
III	465	77.2
IV	138	64.5
V	37	29.7

$TcPO_2 > 900$ mmHg for healing to occur. Table 7 indicates that 900 mmHg may be a very high threshold. Accordingly, it seems logical that an analysis of the combined effects of being below 20 mmHg in air and below 500 mmHg in chamber might provide a superior filter. There were 215 patients with both measurements recorded. Because the cutoff scores in the chamber and in air have been modified, we shall refer to this as the modified Myers and Emhoff analysis. Evaluation of the best combinations of $TcPO_2$ in-chamber and in air cutoff scores requires a grid search, the results of which are presented in Table 8. The PPV is the failure rate in each cell of the table.

The shaded cells in Table 8 seem to be the best choices for discrimination. $TcPO_2$ values below 400 mmHg in the chamber and below 15 mmHg in air may be the best single choice by a small margin, based on the statistics given and considering the sample size. The lower right-hand cell has an excellent PPV, but it is not a good choice because it selects too few patients and has the same failure rate as the cell to its left. Reliability was nearly the same in every cell, hence PPV, sensitivity, and sample size were the controlling factors.

Subsequently, sea-level oxygen data were evaluated in conjunction with the in-chamber readings. The sample size decreased to 168 patients from 215 because 47 of the patients with in-chamber measurements did not have $TcPO_2$ measured in oxygen at sea-level. This smaller sample size made the "at-risk groups" small enough that results were erratic, and hence no analysis is provided.

Modified Wagner score of the worst wound

The Wagner score of the worst wound being treated is another key factor in the ability to predict healing. Table 9 shows the distribution of the highest modified Wagner score for each patient.

From this table it may be seen that wounds with a modified Wagner score of I or II have a high healing rate without reference to secondary factors such as $TcPO_2$. HBO_2T for these patients would be undertaken only if the physician determined that the wound was deteriorating or special wound hypoxia problems were present. Grade V wounds have a poor performance record even with HBO_2T. These patients have extensive gangrenous changes and thus they would normally not be accepted for hyperbaric therapy unless there were compelling reasons, such as to prepare for a limb-saving surgical intervention. Therefore, Wagner Grades III and IV are the most likely to be treated by HBO_2T.

DISCUSSION

The results of a retrospective study are largely dependent on the consistency of the observer in recording data and the accuracy and completeness of the available charts. A multi-institutional database permits a large sample size and reduces the chance of bias that may result from treatment practices at an individual facility. Disadvantages are that different members of the medical staff conducted the evaluations and chart entries; tests (such as $TcPO_2$ measurements) were performed according to varying protocols with instruments that might not have been calibrated to a common standard. This study was strengthened, however, by the fact that one physician observer completed all of the chart audits at the first five clinics, thus omitting any interobserver variation. A second observer compiled the additional data from Travis Air Force Base and Memorial Hermann Hospital. In a multi-institutional database, completeness and quality of information vary among facilities and within the same facility over time, with older charts generally being less well documented than more recent ones. In addition, the objectives of treatment changed somewhat over the years during which these patients were treated. Rather than complete epithelialization, the more contemporary goal is the development of a confluent granulation base from which epithelialization can continue without further hyperbaric therapy. As a consequence, achieving complete healing may not be the best objective for cost-effective treatment of patients with hyperbaric oxygen therapy.

In a study that did not involve the use of hyperbaric therapy, Wyss et al.[21] reported that in postoperative patients, sea-level air $TcPO_2$ readings <20 mmHg were associated with poor healing, 20–40 mmHg with intermediate healing, and >40 mmHg with good healing. However, in our study of 629 hyperbaric patients, 48% of the hyperbaric patients had a baseline $TcPO_2$ below 20 mmHg, yet their failure rate was only 35%. This may suggest the effectiveness of HBO_2T.

In patients with hypoxic wounds as identified by low initial $TcPO_2$, there was no reliable baseline value breathing air at 1 ATA above which healing was ensured or below which failure was uniformly observed. The major reason for the poor performance of the baseline $TcPO_2$ in air at sea-level is the poor correlation it has with $TcPO_2$ in the chamber. High in-chamber $TcPO_2$ values were almost as likely to occur in patients with low sea-level air $TcPO_2$ values as those with high sea-level air values. Therefore, the primary value of sea-level air $TcPO_2$ is to determine whether the wound is likely to heal spontaneously. In this study, patients were generally excluded from hyperbaric treatment if baseline air $TcPO_2$ was greater than 40 mmHg. In the relatively small number of patients with normal baseline $TcPO_2$ who were treated with hyperbaric therapy, there were patients whose wounds were not improved after a course of hyperbaric treatment. Clearly, healing is determined by many factors[21,22] such as nutrition, infection control, glycemic control, smoking history, and other variables that cannot be controlled in a retrospective analysis. However, we emphasize that patients whose $TcPO_2$ is normal are not likely to have hypoxic wounds, and therefore, healing, if impaired, is unlikely to be due to low oxygen levels. Patients with normal values of $TcPO_2$ in air should not be selected for hyperbaric oxygen therapy unless there are mitigating circumstances such as the presence of chronic osteomyelitis, for which the rationale of hyperbaric therapy is different.

Prediction is helped with the addition of sea-level oxygen breathing, as others have observed.[9, 13,15] Patients whose sea-level oxygen $TcPO_2$ is 35 mmHg or greater are likely to benefit from hyperbaric therapy. This agrees with data from a prospective study by Sheffield et al.[18] suggesting that there should be a minimum floor (35 mmHg) for the absolute value of the sea-level oxygen $TcPO_2$ result. Our data suggest that the accuracy of sea-level oxygen in predicting benefit from HBO_2T is approximately 69%. The absolute increase (in mmHg) with oxygen breathing was better than the percent increase (or ratio) over baseline because many patients with a baseline near zero were not healed even if their $TcPO_2$ doubled or tripled (e.g., going from 2 mmHg to 6 mmHg). Because in-chamber transcutaneous testing is not universally available, there are advantages to applying some combination of sea-level air or oxygen readings in outcome prediction. In a recent prospective study of 46 patients, Sheffield et al.[18] showed that a $TcPO_2$ model in which a $TcPO_2$ in air was > 0 mmHg, coupled with an absolute $TcPO_2$ in oxygen >35 mmHg, and an oxygen challenge increase of $>50\%$ was useful in predicting healing.

These data support the use of in-chamber $TcPO_2$ as a screening tool as originally described by Wattel et al.[13] As they have previously observed, the likelihood of healing with in-chamber $TcPO_2$s below 100 mmHg is very low, whereas the healing rate is extremely high for patients whose in-chamber $TcPO_2$ is 500 mmHg or greater. Our data suggest that an in-chamber $TcPO_2$ of 200 mmHg may be the most valuable cutoff.

It must be remembered that the value of a cutoff score is determined by its use. If our goal is the most cost-effective use of HBO_2T, then we should screen out patients destined to fail. Using sea-level oxygen breathing as a screen has an accuracy approaching 70%. The accuracy of in-chamber $TcPO_2$ approaches 75%. However, even with such screening tools, our prediction would still be incorrect in one out of four cases, and patients who might benefit from HBO_2T would be deprived of therapy. Therefore, these cutoff scores must serve as guides to therapy. A rational approach may be to provide a trial of therapy and then reassess patients on the basis of clinical progress or improved $TcPO_2$s. This should be the basis for further investigation.

To our knowledge, this retrospective analysis represents the largest accumulation of hyperbaric patients ever collected. Given the cost and limited availability of hyperbaric therapy, all prospective controlled trials have involved relatively small numbers of patients. Previous prospective studies evaluating the predictive value of $TcPO_2$ have included fewer than 100 patients per study. These small sample sizes have precluded evaluation of the accuracy and predictive value of $TcPO_2$. Furthermore, $TcPO_2$ data acquired in controlled laboratory settings may differ from those obtained in the typical clinical setting. Although our $TcPO_2$ data are pooled from several centers, we feel they reflect the type of data commonly collected by wound and hyperbaric medicine centers, and the large volume of samples outweighs the small differences in technique.

We summarize the results of this analysis as follows:

- The $TcPO_2$ value measured at sea-level in air has almost no predictive value with regard to the benefit of subsequent HBO_2T. Baseline $TcPO_2$ measurement in air is of value for confirming that a wound is hypoxic and therefore at increased risk for wound healing failure in the absence of hyperbaric oxygen therapy.
- Sea-level $TcPO_2$ oxygen data do have some predictive value. When the $TcPO_2$ breathing oxygen is below 35 mmHg, the failure rate is 41%. The accuracy of this test in predicting outcome after hyperbaric therapy is approximately 69%.
- The $TcPO_2$ value measured in-chamber during hyperbaric oxygen breathing provides the best single discriminator between success and failure of hyperbaric therapy using a cutoff score of 200 mmHg. This test is 74% reliable.
- A combination of in-chamber $TcPO_2$ and sea-level air $TcPO_2$ may increase accuracy slightly by improving PPV.

This study does not directly show the effectiveness of HBO_2T because there was no control group of similar patients who did not receive the therapy. For many patients, however, HBO_2T was the only alternative to amputation and in light of this, the overall success rate of 75.6% in a large series of patients with modified Wagner III and IV lesions is encouraging.

Based on the above data, we would make the following suggestions for the practical use of $TcPO_2$ in patient selection for hyperbaric oxygen therapy:

- Baseline air $TcPO_2$ should be performed to determine whether tissue hypoxia exists.
- In the absence of in-chamber $TcPO_2$ data, measuring the absolute $TcPO_2$ breathing sea-level oxygen may be of value in determining whether subsequent HBO_2T will be of benefit.
- Whenever possible, in-chamber $TcPO_2$ data should be utilized as a guide to patient selection for HBO_2T.

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APPENDIX

Participating units: the Southeast Texas Center for Wound Care and Hyperbaric Medicine, at Conroe Regional Medical Center, Conroe, Texas; the Jefferson C. Davis Wound Care and Hyperbaric Medicine Center at South-west Texas Methodist Hospital, San Antonio, Texas; the Nix Wound Care and Hyperbaric Medicine Facility at Nix Medical Center, San Antonio, Texas; The University of Texas Medical Branch Hyperbaric Medicine Center, Galveston, Texas; the Memorial Hermann Hospital Center for Hyperbaric Medicine, Houston, Texas; and The Hyperbaric Medicine Department at Travis Air Force Base, California.

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