



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

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The objective of this retrospective analysis was to determine the reliability of transcutaneous oxygen tension measurement (TcPO₂) in predicting outcomes of diabetics who underwent hyperbaric oxygen therapy for lower extremity wounds. Six hyperbaric facilities provided TcPO₂ 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 TcPO₂ 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 TcPO₂ values. Breathing oxygen at sea level was unreliable for predicting failure, but 68% reliable for predicting success after hyperbaric oxygen therapy. TcPO₂ 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 TcPO₂ 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 TcPO₂ < 15 mmHg combined with an in-chamber TcPO₂ < 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)

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ATA	Atmosphere absolute
HBO ₂ T	Hyperbaric oxygen therapy
PPV	Positive predictive value
TcPO ₂	Transcutaneous oxygen tension

Hyperbaric oxygen therapy (HBO₂T) 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 HBO₂T can supply tissues with adequate oxygen to support metabolism, even if the vascular supply is compromised.¹ As a result, HBO₂T 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 HBO₂T in diabetic ulcers of the lower extremity.²⁻⁷ The economic and emotional costs of amputation and rehabilitation easily exceed the cost of

HBO₂T 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 HBO₂T candidates.⁹ The objective of our analysis was to determine the accuracy and predictive value of transcutaneous oxygen tension (TcPO₂) in predicting the likelihood of benefit or failure of HBO₂T, using data from a very large series of patients.

The technique of TcPO₂ measurement has been well described⁹ 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 HBO₂T,¹³ but small sample sizes have limited the ability to assess the accuracy and reliability of TcPO₂. A variety of techniques have been employed to enhance the predictive value of TcPO₂. Observing the absolute value and the relative increase in TcPO₂ while breathing oxygen at sea level seems to increase the accuracy of TcPO₂ 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 TcPO₂ has previously been shown to have the strongest statistical relationship to benefit from HBO₂T.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 scale¹⁷ 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 HBO₂T. 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 HBO₂T 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 epithelialization, 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 HBO₂T 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.

TcPO₂ 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 TcPO₂ 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 TcPO₂, the absolute increase in mmHg over the sea-level air TcPO₂, and the percent increase compared with the air TcPO₂. Because in-chamber TcPO₂ is a relatively recent development, not all patients underwent in-chamber TcPO₂ 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 TcPO₂ measurements were developed as part of the analytical process. These included combinations of factors such as baseline air TcPO₂ in conjunction with in-chamber TcPO₂, originally described by Myers and Emhoff,¹⁹ and the effects of Wagner score on the predictive value of TcPO₂.

We employed the following definitions with respect to using TcPO₂ 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 HBO₂T. 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 HBO₂T. Patients who improved after HBO₂T received a mean of 34 treatments, while those who did not

improve received a mean of 24 treatments, apparently because HBO₂T was discontinued if the patient did not appear to be improving. In 77% of improved patients, HBO₂T 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 HBO₂T (*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 HBO₂T 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 TcPO₂ in air and in sea-level oxygen, the interrupted group averaged nine more HBO₂Ts 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 HBO₂T 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 HBO₂T 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

Wound status at follow-up	Outcome class at termination of HBO ₂ T				Totals (%)
	Healed (%)	Partial healing (%)	No healing (%)	Amputation (%)	
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 ₂ T to follow-up (wks)					
Median	2	4	4	2	
75th percentile	8	15	8	3.5	

n = 756 patients.

Table 2. Sea-level TcPO₂ 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 HBO₂T, 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 TcPO₂ 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 TcPO₂s 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 TcPO₂s.

TcPO₂ data

Sea-level air TcPO₂ data for the 629 patients are presented in Table 2. The purpose of the sea-level air TcPO₂ 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 HBO₂T compared with those having a TcPO₂ < 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 HBO₂T might not be expected) fewer than half the patients predicted to fail actually failed.

Sea-level TcPO₂ breathing oxygen data

Table 3 shows the absolute TcPO₂ 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 TcPO₂ 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 TcPO₂ 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 TcPO₂ 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 TcPO₂ 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 TcPO₂ during oxygen challenge. A decrease (or no increase) in TcPO₂ 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 TcPO₂ 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 TcPO₂ 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 TcPO₂ from baseline is seen to perform no better than the absolute level of TcPO₂ 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 TcPO₂ value while breathing sea-level oxygen is the most useful of the various methods of analyzing sea-level TcPO₂ 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 TcPO₂ measurements

In-chamber TcPO₂ readings were taken on a subset of 221 patients. Table 6 reports the statistics associated with alternative cutoff scores. Of those with in-chamber TcPO₂ levels < 100 mmHg, only 10% of patients were better after HBO₂T. Of those with in-chamber TcPO₂ levels > 500 mmHg, 78.8% were improved after HBO₂T. 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 TcPO₂ 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.

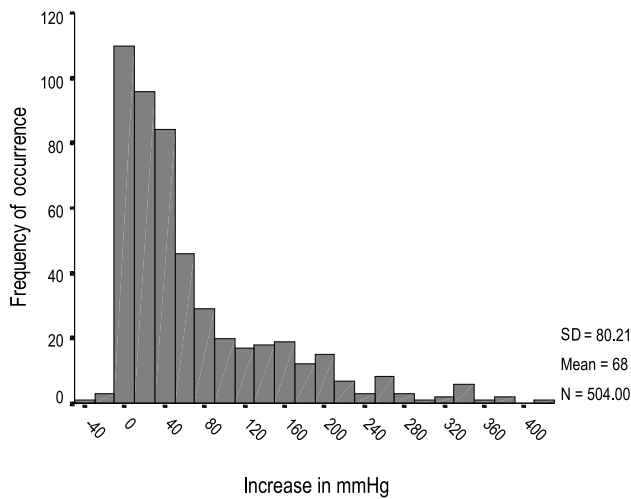


FIGURE 1. Distribution of TcPO₂ values during sea-level oxygen breathing.

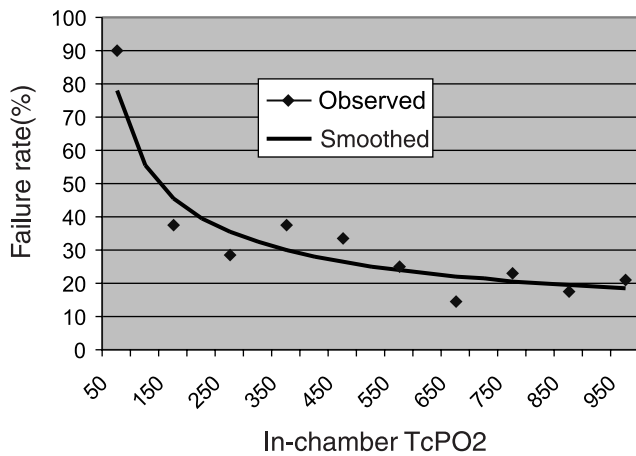


FIGURE 2. Estimate of the failure rate of HBO₂T in relation to in-chamber TcPO₂. Failure rate increases as in-chamber TcPO₂ decreases. However, as in-chamber TcPO₂ increases above 400 mmHg, there is little incremental improvement in healing likelihood.

group large enough to make screening worthwhile. If the in-chamber TcPO₂ is less than 200 mmHg, then the likelihood of failure is at least 58%. It appears that once some threshold

Table 7. In-chamber TcPO₂ 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.

value of in-chamber TcPO₂ 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 TcPO₂ 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 TcPO₂ ranges. A smooth curve through the data provides a better picture of the relationship between decreasing in-chamber TcPO₂ 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 (TcPO₂)^{-0.492}; R² = 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 TcPO₂ value.

Myers and Emhoff-type analysis

Myers and Emhoff¹⁹ studied a small set of diabetic patients (n = 11) and concluded that for estimating between success and failure, those patients whose TcPO₂ in air was < 20 mmHg would need an in-chamber

Table 6. In-chamber TcPO₂ 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 TcPO₂ versus in-chamber TcPO₂ as a screening tool for failure of hyperbaric oxygen therapy

In air at sea-level	In-chamber		
	< 500 mmHg	< 400 mmHg	< 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 HBO₂T

Wagner score	Sample size	Helped by HBO ₂ T (%)
I	3	100.0
II	130	83.1
III	465	77.2
IV	138	64.5
V	37	29.7

TcPO₂ > 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 TcPO₂ 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. TcPO₂ 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 TcPO₂ 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 TcPO₂. HBO₂T 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 HBO₂T. 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 HBO₂T.

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 TcPO₂ 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 TcPO₂ 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 TcPO₂ below 20 mmHg, yet their failure rate was only 35%. This may suggest the effectiveness of HBO₂T.

In patients with hypoxic wounds as identified by low initial TcPO₂, 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 TcPO₂ in air at sea-level is the poor correlation it has with TcPO₂ in the chamber. High in-chamber TcPO₂ values were almost as likely to occur in patients with low sea-level air TcPO₂ values as those with high sea-level air values. Therefore, the primary value of sea-level air TcPO₂ is to determine whether the wound is likely to heal spontaneously. In this study, patients were generally excluded from hyperbaric treatment if baseline air TcPO₂ was greater than 40 mmHg. In the relatively small number of patients with normal baseline TcPO₂ 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 TcPO₂ 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 TcPO₂ 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 TcPO₂ 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 TcPO₂ result. Our data suggest that the accuracy of sea-level oxygen in predicting benefit from HBO₂T 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 TcPO₂ 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 TcPO₂ model in which a TcPO₂ in air was > 0 mmHg, coupled with an absolute TcPO₂ in oxygen >35 mmHg, and an oxygen challenge increase of >50% was useful in predicting healing.

These data support the use of in-chamber TcPO₂ as a screening tool as originally described by Wattel et al.¹³ As they have previously observed, the likelihood of healing with in-chamber TcPO₂s below 100 mmHg is very low, whereas the healing rate is extremely high for patients whose in-chamber TcPO₂ is 500 mmHg or greater. Our data suggest that an in-chamber TcPO₂ 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 HBO₂T, 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 TcPO₂ 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 HBO₂T 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 TcPO₂s. 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 TcPO₂ have included fewer than 100 patients per study. These small sample sizes have precluded evaluation of the accuracy and predictive value of TcPO₂. Furthermore, TcPO₂ data acquired in

controlled laboratory settings may differ from those obtained in the typical clinical setting. Although our TcPO₂ 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 TcPO₂ value measured at sea-level in air has almost no predictive value with regard to the benefit of subsequent HBO₂T. Baseline TcPO₂ 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 TcPO₂ oxygen data do have some predictive value. When the TcPO₂ 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 TcPO₂ 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 TcPO₂ and sea-level air TcPO₂ may increase accuracy slightly by improving PPV.

This study does not directly show the effectiveness of HBO₂T because there was no control group of similar patients who did not receive the therapy. For many patients, however, HBO₂T 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 TcPO₂ in patient selection for hyperbaric oxygen therapy:

- Baseline air TcPO₂ should be performed to determine whether tissue hypoxia exists.
- In the absence of in-chamber TcPO₂ data, measuring the absolute TcPO₂ breathing sea-level oxygen may be of value in determining whether subsequent HBO₂T will be of benefit.
- Whenever possible, in-chamber TcPO₂ data should be utilized as a guide to patient selection for HBO₂T.

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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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