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Hyperbaric oxygen therapy in necrotising soft tissue infections: a study of patients in the United States Nationwide Inpatient Sample

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Abstract *Purpose:* Necrotising soft tissue infection (NSTI) is a deadly disease associated with a significant risk of mortality and long-term disability from limb and tissue loss. The aim of this study was to determine the effect of hyperbaric oxygen (HBO_2) therapy on mortality, complication rate, discharge status/location, hospital length of stay and inflation-adjusted hospitalisation cost in patients with NSTI. *Methods:* This was a retrospective study of 45,913 patients in the Nationwide Inpatient Sample (NIS) from 1988 to 2009. *Results:* A total of 405 patients received HBO_2 therapy. The patients with NSTI who received HBO_2 therapy had a lower mortality (4.5 vs. 9.4 %, $p = 0.001$). After adjusting for predictors and confounders, patients who received HBO_2 therapy had a statistically significantly lower risk of dying (odds ratio (OR) 0.49, 95 % confidence interval (CI) 0.29–0.83), higher hospitalisation cost (US$52,205 vs. US$45,464, $p = 0.02$) and longer length of stay (LOS) (14.3 days vs. 10.7 days, $p < 0.001$). *Conclusions:* This retrospective analysis of HBO_2 therapy in NSTI showed that despite the higher hospitalisation cost and longer length of stay, the statistically significant reduction in mortality supports the use of HBO_2 therapy in NSTI.

Keywords Hyperbaric oxygen therapy · Healthcare cost and utilisation project · National inpatient sample · Necrotising soft tissue infections

Introduction

Necrotising soft tissue infections (NSTI) are associated with mortality rates ranging from 0 to 73 % [1–3]. In addition, they can lead to significant morbidity such as limb amputations. Early surgical debridement and antibiotics remain the mainstay of management, but hyperbaric oxygen therapy (HBO_2 therapy) has been used as an adjunct. Although there are many uncontrolled case series [4] and expert opinions about the role of HBO_2 therapy in NSTI, as far as we know, no controlled studies have been conducted with a sample size greater than 80 [5]. Published articles have repeatedly stated that there is a lack of evidence for the effectiveness of HBO_2 therapy in NSTI and thus it is not uncommon to read about statements describing the lack of adequately powered or controlled trials in HBO_2 therapy for NSTI [4, 6, 7]. The rarity of these conditions [8] and their high acuity make

prospective randomised studies difficult to perform, and these are unlikely ever to occur. A recent review stated that the weakness of previous studies precludes a meta-analysis to resolve contradictory findings and a firm recommendation on the use of HBO_2 therapy for NSTI cannot be made until better designed studies are conducted [7]. It is to address exactly this point that the current study was performed.

Materials and methods

Methods

Ethics approval was obtained from the National University of Singapore's institutional review board. The study involved secondary analysis of the dataset in the Nationwide Inpatient Sample (NIS) database which avoids any linkage to individual patients and effectively anonymizes the patients captured in the dataset. The NIS is an all-payer inpatient care database that is part of the Healthcare Cost and Utilisation Project (HCUP) of the Agency for Healthcare Research and Quality in the USA. It captures information such as mortality, charges and hospital length of stay (LOS) from 1,044 hospitals in 40 states in the USA. The database reflects a 20 % stratified sample of community hospitals. On the basis of the American Hospital Association definition of a community hospital, this includes public hospitals and academic medical centres. It does not include federal hospitals (mostly veterans administration hospitals) or hospital units of institutions such as prisons and infirmaries. The NIS database effectively incorporates 90 % of all hospital discharges in the USA between 1988 and 2009. It contains data on more than 7,000,000 hospital stays which makes it the largest database of its kind in the USA. It has been used to track healthcare trends and also provides a valuable resource for research into uncommon diseases. A maximum of 15 diagnoses and 15 procedures can be captured in its data set. However the actual number recorded varies from state to state. This study compared the mortality, complications, hospital LOS, hospitalisation cost, discharge status and location of patients with NSTI who received HBO_2 therapy versus those who did not. We performed a retrospective study on patients in the NIS database from 1988 to 2009. The templates and material developed by the Research on Research group, for formulating a research question (Question Diagram) and writing the manuscript, while conducting this secondary data analysis/study were used [9, 10]. All patients in the NIS database who have NSTI were included in the study. Patients were identified using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. The ICD-9-CM is derived from the World Health Organisation's Ninth Revision of the International Classification of Diseases (ICD-9). Patients meeting the inclusion criteria were selected using ICD-9-CM codes for necrotising fasciitis, Fournier's and gas gangrene. Patients who received HBO_2 therapy formed one group and those who did not receive HBO_2 therapy formed the control group.

Outcomes

In-hospital mortality was the primary outcome. Secondary outcomes included the disposition of the patient (discharge status and location), hospital LOS, total inflation-adjusted hospital charges, complications related to NSTI including limb loss (amputations), tissue loss (revision of amputation stump), cardiovascular collapse, cardiac arrest, cardiac complications (cardiac arrest or failure following anaesthesia), acute myocardial infarction, shock, respiratory arrest, pulmonary embolism, pneumonia, cerebrovascular accidents (CVA), severe sepsis (sepsis with acute organ dysfunction, sepsis with multiple organ dysfunction (MOD), systemic inflammatory response syndrome due to infectious process with acute organ dysfunction) and acute organ dysfunction (acute renal failure, acute and chronic respiratory failure, critical illness myopathy/polyneuropathy, disseminated intravascular coagulation, metabolic encephalopathy, acute hepatic failure, septic shock, heart failure), complications related to HBO_2 therapy including ear barotrauma, seizures, pneumothoraces, and hypoglycemia. The discharge can be routine or non-routine. A non-routine discharge includes discharge to a short-term hospital, skilled nursing facility, intermediate care facility, another type of facility, home health care, against medical advice or death. The hospitalisation cost was adjusted for inflation by multiplying it by the inflation factor for the corresponding year. Complications were identified by searching all diagnosis and procedure fields for the ICD-9-CM codes.

Predictors and confounders

The ICD-9-CM procedure codes for hyperbaric oxygenation and decompression chamber were used to identify the patients in the HBO_2 therapy group; all the other patients were assigned to the non-HBO_2 therapy group.

Possible confounders included age, gender, the patient's county of residence, hospital characteristics (bed size, location and teaching status), and the Deyo clinical co-morbidity index. This index is a weighting of various conditions including myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, mild liver disease, diabetes, diabetes with chronic complications, hemiplegia

or paraplegia, renal disease, any malignancy, including leukaemia and lymphoma, moderate or severe liver disease, metastatic solid tumour and AIDS [11]. These co-morbid conditions were identified using the ICD-9-CM diagnosis and procedure codes.

The patients were stratified according to the key confounders such as the admission source, admission type, site of infection and aetiology of infection. Patients were stratified to truncal/extremity NSTI, traumatic/spontaneous NSTI, clostridial myonecrosis/non-clostridial NSTI, admission source and admission type.

Patients with truncal NSTI were identified by searching all the procedure fields in the NIS database for the ICD-9-CM procedure codes that correspond to operations in the truncal region. Similarly, patients with extremity NSTI were identified by searching for the procedure codes corresponding to limb amputations. Patients with trauma-related NSTI were identified by searching for the ICD-9-CM diagnosis codes that correspond to trauma. All other patients were grouped into the non-traumatic NSTI group.

Patients with clostridial myonecrosis were identified by searching for the ICD-9-CM diagnosis code that corresponds to gas gangrene. Patients with non-clostridial myonecrosis were identified using the codes for necrotising fasciitis and Fournier's gangrene.

Statistical analysis

The two-sample *t* test was used to compare the ages of the HBO_2 therapy and non-HBO_2 therapy groups. The two-sample Wilcoxon rank-sum (Mann–Whitney) test was used to compare the LOS and total inflation-adjusted hospital charges. The Pearson chi-squared test was used to test association between the confounders (gender, discharge, hospital size, type of hospital, Deyo co-morbidity index, admission type, admission source, site of NSTI, aetiology of NSTI), the outcomes (mortality, amputations, need for revision of stump, complications) and predictor (HBO_2 therapy and non-HBO_2 therapy group). Multivariate logistic regression was used to adjust for known confounders when calculating the odds ratio (OR). Quantile regression was used to determine the adjusted medians for the LOS and inflation-adjusted hospital charges. In order to reduce potential bias due to an imbalance in patient characteristics between the HBO_2 therapy and non-HBO_2 therapy groups, a propensity score [12] was derived using a logistic regression for predictor (HBO_2 therapy vs. non-HBO_2 therapy) as the dependent variable and the aforementioned set of confounders as the independent variables. All the multivariate logistic and quantile regressions for the outcome variables were adjusted for this propensity score. A p value less than 0.05 was considered to be statistically significant. Data from patients with missing values were not analysed. The data were analysed using the Stata/SE 9.2 (Stata Corp., College Station, TX, USA) statistical software.

Results

A total of 45,913 patients were diagnosed with NSTI in the NIS database, of whom 405 (0.88 %) received HBO_2 therapy. The demographics and disposition of the patients are presented in Table 1. The patients who received HBO_2 therapy had more co-morbidities based on the Deyo scoring system. In addition, these patients were more likely to be in a larger, urban hospital. Fewer of the patients who received HBO_2 therapy were emergency admissions. There was no statistically significant difference in the anatomical site or the probability that the disease was trauma-related.

Patients who received HBO_2 therapy had a lower mortality and complications related to NSTI (Table 2). However they were more likely to have a longer LOS in the hospital and higher cost for their hospitalisations. None of the patients who received HBO_2 therapy were reported to have complications associated with HBO_2 therapy (ear barotrauma, seizures, pneumothorax, hypoglycemia). Using the propensity score as a balancing score, patients who received HBO_2 therapy had a lower mortality (OR 0.49, 95 % confidence interval (CI) 0.29–0.83, $p = 0.008$). Both groups were equally likely to have a routine discharge and to develop complications related to NSTI. The adjusted median LOS was 14.3 days (95 % CI 13–16) for the patients who received HBO_2 therapy versus 10.7 days (95 % CI 10–11) for the patients who did not receive HBO_2 therapy ($p < 0.001$). A subgroup analysis of patients who survived to hospital discharge was performed and the adjusted median LOS for the survivors was 14.1 days (95 % CI 12.9–15.4) for those who received HBO_2 therapy versus 10.7 days (95 % CI 10.6–10.9) for those who did not receive HBO_2 therapy ($p < 0.001$). However, for the patients who died in hospital, the adjusted median duration of survival was 17.1 days (95 % CI 9.7–24.4) for those who received HBO_2 therapy versus 8.8 days (95 % CI 8.2–9.3) for those who did not receive HBO_2 therapy ($p = 0.03$). The adjusted median cost was US$52,205 (95 % CI US$46,397–58,012) for those who received HBO_2 therapy versus US$45,464 (95 % CI US$44,867–46,060) for those who did not receive HBO_2 therapy ($p < 0.001$). Tables 3 and 4 show the outcomes after stratification.

Discussion

There was no difference in the rate of complications in the two groups following adjustment using the propensity score. Patients in the HBO_2 therapy group had a longer adjusted median hospital LOS and a higher adjusted

Table 1 Demographics and baseline characteristics of the HBO_2 therapy group (HBOT) and the non-HBO_2 therapy group (control)

	HBOT ($n = 405$)	Control ($n = 45{,}508$)	p value
Mean age, years (95 % CI)	54.6 (53.2–56.1)	53.7 (53.6–53.9)	0.23
Gender			0.03*
Male	243 (60.0)	29,612 (65.1)	
Female	162 (40.0)	15,885 (34.9)	
Hospital bed size			0.02*
Small	33 (8.2)	5,359 (11.8)	
Medium	124 (30.6)	11,818 (26.0)	
Large	248 (61.2)	28,219 (62.2)	
Location/teaching status of hospital			<0.001*
Rural	16 (4.0)	4,865 (10.7)	
Urban non-teaching	222 (54.8)	18,621 (41.0)	
Urban teaching	167 (41.2)	21,910 (48.3)	
Deyo category [12]			0.05*
0	144 (35.6)	18,925 (41.6)	
1	129 (31.9)	12,808 (28.1)	
>1	132 (32.6)	13,775 (30.3)	
Admission type			<0.001*
Emergency	162 (43.4)	23,705 (59.9)	
Urgent	111 (29.8)	9,316 (23.5)	
Elective	92 (24.7)	6,344 (16.0)	
Newborn	0	81 (0.2)	
Others	≤10[b]	122 (0.3)	
Admission source			<0.001*
Emergency room	147 (39.4)	21,976 (57.6)	
Another hospital	47 (12.6)	3,411 (8.9)	
Another facility including long-term care	19 (5.1)	969 (2.5)	
Court/law enforcement	0	36 (0.1)	
Routine/birth/other[a]	160 (42.9)	11,750 (30.8)	
Site of NSTI			
Truncal	19 (4.7)	1,491 (3.3)	0.10
Extremity	57 (14.1)	6,681 (14.7)	0.73
Mechanism of NSTI			0.75
Traumatic	≤10[b]	1,018 (2.2)	
Non-traumatic	395 (97.5)	44,490 (97.8)	
Pathogen for NSTI			0.005*
Clostridial myonecrosis	66 (16.3)	10,032 (22.0)	
Non-clostridial myonecrosis	339 (83.7)	35,476 (78.0)	

Data are presented as n (%) unless otherwise specified. Containment System (AHCCCS)

* Statistically significant

[a] Includes deliveries, patients referred from clinics, outpatient services, health maintenance organization (HMO) and the Arizona Health Care Cost

[b] HCUP privacy protection requirements do not allow the reporting of data where there are less than or equal to 10 individual records in a given cell

median hospitalisation cost. The longer LOS among the subgroup of survivors in the HBO_2 therapy group compared to the control group demonstrates that this could not be attributed to a difference in survival duration. Another study reported higher average daily costs for patients receiving HBO_2 therapy although there was no statistically significant difference in total costs [8]. The difference in adjusted median cost in our study is US$6,741, probably due largely to the cost of HBO_2 therapy and the longer LOS in the HBO_2 therapy group. It is not possible to determine how much of the additional cost is attributable to HBO_2 therapy as the NIS database does not capture the number of HBO_2 therapy sessions.

In this study, patients with clostridial myonecrosis did not seem to benefit from HBO_2 therapy which is not consistent with the findings in previous studies [13]. A possible explanation may be that for this subset, the study is underpowered: only 66 of the 10,098 patients with clostridial myonecrosis received HBO_2 therapy in the database. Patients with non-clostridial myonecrosis who received HBO_2 therapy had a lower mortality. However there was a higher hospitalisation cost and longer LOS. Other studies have also reported improved outcomes with HBO_2 therapy in non-clostridial myonecrosis [14]. Despite the size of this study it is still underpowered to test the effect of HBO_2 therapy in specific subgroups such as extremity versus truncal infection.

There are many animal studies suggesting possible mechanisms of benefit of HBO_2 therapy in NSTI. Proposed mechanisms include improved oxygenation [15,

Table 2 Results of bivariate analysis showing outcomes in the HBO_2 therapy and non-HBO_2 therapy groups

	HBOT	Control	*p* value
In-house mortality	18 (4.5)	4,289 (9.4)	0.001*
Complications related to NSTI	131 (32.4)	16,949 (37.2)	0.04*
Amputations	57 (14.1)	6,681 (14.7)	0.73
Revision of amputation stump[a]	≤10	1,345 (3.0)	
Cardiovascular collapse[a]	≤10	96 (0.2)	
Cardiac arrest	≤10	580 (1.3)	
Cardiac arrest or failure following anaesthesia[a]	0	0	
Acute myocardial infarction	0	≤10	
Shock	20 (4.9)	4,027 (8.9)	0.01*
Respiratory arrest[a]	≤10	49 (0.1)	
Pulmonary embolism[a]	0	16 (0.04)	
Pneumonia	17 (4.2)	2,418 (5.3)	0.32
CVA[a]	≤10	298 (0.7)	
Severe sepsis	14 (3.5)	3,274 (7.2)	0.004*
Acute organ dysfunction	65 (16.1)	9,891 (21.7)	0.006*
Discharge status			0.14
Routine	137 (35.6)	16,006 (39.3)	
Non-routine[b]	248 (64.4)	24,760 (60.7)	
Inflation-adjusted cost, US$	107,865	86,892	<0.001*

Data are presented as *n* (%) or *n* unless otherwise specified

* Statistically significant

[a] HCUP privacy protection requirements do not allow the reporting of data where there are less than or equal to 10 individual records in a given cell

[b] Non-routine discharge includes discharge to a short-term hospital, skilled nursing facility, intermediate care facility, another type of facility, home health care, against medical advice or death

16], inhibition of anaerobic infections [17], oedema reduction [18], enhanced white cell action [19–24], elevation of superoxide dismutase levels [25], reducing systemic inflammation [26], increased effectiveness of antimicrobial agents [27], inhibition of alpha-toxin production [28] and growth of clostridial organisms [29]. During later stages, HBO_2 therapy improves angiogenesis [30], fibroblast activity and collagen synthesis [31], thereby promoting wound healing.

There are many studies supporting the use of HBO_2 therapy in NSTI [13, 14, 32]. However, there are also studies which have not shown any survival benefit [4, 5, 33]. One possible explanation is that these earlier studies may not have been adequately powered [6]. There are few published collective reviews and these mostly contain insufficient detail to do a retrospective case–control study. In addition, the number of HBO_2 therapy sessions may have been too few for it be beneficial [33]. The failure to adjust for significant predictors and confounders in many of these studies could also have accounted for the negative results [4].

Limitations of the study

Although we may not have included every possible complication in the analysis, it is unlikely that the rarer complications would have affected the result. The NIS database does not capture several predictors and confounders for the outcome of patients with NSTI. This includes the time to diagnosis [34], performance of a tissue biopsy (which could speed up the diagnosis [35], time to surgical debridement [4, 36], number and adequacy of surgical debridement [37], body surface area involved/extent of the NSTI [4], hyperlactataemia [4], number of HBO_2 therapy sessions, immune globulin use [38], antibiotic use, physiologic parameters and diseases on admission (white blood cell count, haematocrit, creatinine levels, heart disease and the presence of shock), multiple-organ dysfunction syndrome (MODS) scores, Acute Physiology and Chronic Health Evaluation (APACHE) II scores [39] and whether they were ICU admissions or not. Thus it is not possible to analyse the effect of these confounders on the outcomes. The lack of data regarding the number of HBO_2 therapy sessions makes it impossible to estimate a dose–response which could strengthen the notion of a true treatment effect. On the other hand, despite the lack of consensus about the optimal number of treatment sessions for NSTI [6], most HBO_2 therapy treatments for NSTI are short-term in nature, averaging 3–10 sessions [14, 32]. Thus this may not be a significant confounding factor. As the NIS database only captures hospital mortality, there is no information available on patients who die following hospital discharge. This may explain the lower mortality rates in the current study as compared to studies with longer follow-up [8]. Another possible limitation is the accuracy of the coding for the various diagnoses. This could lead to failure to include patients into the analysis which will affect the results. Nevertheless, the NIS database still provides the largest sample of patients with NSTI

Table 3 Adjusted odds ratio (OR) for death and complications with HBO_2 therapy after stratification (using the non-HBO_2 therapy group as the reference group)

	Mortality with HBO_2 therapy (n, %)	Mortality without HBO_2 therapy (n, %)	p value	Unadjusted OR for death (95 % CI)	p value	Adjusted OR for death (95 % CI)	p value
Admission source							
Emergency[a]	≤10	2,338 (10.7)		0.55 (0.28–1.07)	0.08	0.61 (0.30–1.27)	0.19
Another hospital[a]	≤10	397 (11.7)		0.71 (0.25–1.97)	0.50	0.56 (0.17–1.85)	0.34
Another facility including long-term care[a]	0	137 (14.2)					
Court/law enforcement[a]	0	≤10					
Routine/birth/other[a]	≤10	787 (6.7)		0.45 (0.18–1.10)	0.08	0.39 (0.14–1.05)	0.06
Admission type							
Emergency[a]	≤10	2,461 (10.4)		0.45 (0.22–0.91)	0.03*	0.50 (0.24–1.03)	0.06
Urgent[a]	≤10	793 (8.5)		0.40 (0.15–1.09)	0.07	0.45 (0.16–1.24)	0.12
Elective[a]	≤10	342 (5.4)		0.19 (0.03–1.40)	0.10	0.24 (0.03–1.76)	0.16
Newborn[a]	0	≤10					
Other[a]	≤10	16 (13.1)		2.21 (0.41–11.90)	0.36		
Pathogen							
Clostridial myonecrosis[a]	≤10	932 (9.3)		0.97 (0.42–2.26)	0.95	1.16 (0.45–2.98)	0.76
Non-clostridial myonecrosis	12 (3.6)	3,357 (9.5)	<0.001*	0.35 (0.20–0.63)	<0.001*	0.38 (0.20–0.73)*	0.003*
Site							
Extremity[a]	≤10	481 (7.2)					
Truncal[a]	≤10	128 (8.6)		1.25 (0.29–5.47)		1.89 (0.41–8.79)	0.42
Mechanism							
Traumatic[a]	≤10	115 (11.3)		0.87 (0.11–6.93)	0.90		
Non-traumatic	≤10	4,174 (9.4)		0.43 (0.27–0.71)	0.001*	0.47 (0.28–0.82)*	0.007*
	Complication rates with HBO_2 therapy (n, %)	Complication rates without HBO_2 therapy (n, %)	p value	Unadjusted OR for complications (95 % CI)	p value	Adjusted OR for complications (95 % CI)	p value
Admission source							
Emergency[a]	52 (35.4)	8,715 (39.7)	0.29	0.83 (0.59–1.17)	0.29	0.69 (0.47–1.02)	0.06
Another hospital[a]	15 (31.9)	1,210 (35.5)	0.61	0.85 (0.46–1.58)	0.61	0.76 (0.39–1.49)	0.43
Another facility including long-term care[b]	≤10	337 (34.8)		1.09 (0.43–2.80)	0.85	1.47 (0.54–4.00)	0.45
Court/law enforcement[a]	0	≤10					
Routine/birth/other[a]	44 (27.5)	3,320 (28.3)	0.83	0.96 (0.68–1.37)	0.83	1.00 (0.69–1.45)	0.99
Admission type							
Emergency[a]	52 (32.1)	9,991 (42.2)	0.01*	0.65 (0.47–0.90)	0.01*	0.71 (0.50–1.02)	0.06
Urgent[a]	36 (32.4)	3,056 (32.8)	0.93	0.98 (0.66–1.47)	0.93	0.98 (0.63–1.50)	0.91
Elective[a]	22 (23.9)	1,665 (26.3)	0.61	0.88 (0.55–1.43)	0.61	1.03 (0.60–1.75)	0.92
Newborn[a]	0	≤10					
Other[a]	≤10	45 (36.9)		1.03 (0.23–4.50)	0.97	0.72 (0.15–3.58)	0.69
Pathogen							
Clostridial myonecrosis[a]	40 (60.6)	5,556 (55.4)	0.40	1.24 (0.76–2.03)	0.40	1.06 (0.60–1.86)	0.84
Non-clostridial myonecrosis	91 (26.8)	11,393 (32.1)	0.04*	0.78 (0.61–0.99)	0.04*	0.79 (0.60–1.05)*	0.10
Site							
Extremity[a]	57 (100.0)	6,681 (100.0)					
Truncal[a]	≤10	469 (31.5)		1.01 (0.38–2.66)		1.49 (0.52–4.33)	0.46
Mechanism							
Traumatic[a]	≤10	407 (40.0)		1.00 (0.28–3.57)	1.00	0.80 (0.18–3.61)	0.69
Non-traumatic	127 (32.2)	16,542 (37.2)	0.04*	0.80 (0.65–0.99)	0.04*	0.86 (0.67–1.10)	0.23

* Statistically significant

[a] HCUP privacy protection requirements do not allow the reporting of data where there are less than or equal to 10 individual records in a given cell

undergoing HBO_2 therapy. It is conceivable that selection bias may have occurred as a result of varying availability of HBO_2 therapy in different types of treatment facilities (e.g. community hospitals vs. urban medical centres) and varying severity of illness of the NSTI (e.g. emergency, urgent admission vs. elective). However, these were identified as possible confounders and included in the propensity score. Although HBO_2 therapy has been shown to be safe in critically ill patients [40], it is possible that this was withheld from some patients who were deemed

Table 4 Adjusted LOS and cost for HBO_2 therapy after stratification

	Adjusted median LOS, days (95 % CI)		*p* value	Adjusted median hospitalisation cost (95 % CI), US$		*p* value
	HBOT	Control		HBOT	Control	
Admission source						
Emergency	13.9 (11.9–15.9)	10.8 (10.7–11.0)	0.003*	63,425 (53,198–73,651)	48,374 (47,524–49,223)	0.004*
Another hospital	11.1 (5.2–17.1)	17.1 (16.3–17.9)	0.05	50,728 (28,329–73,126)	67,067 (64,230–69,903)	0.16
Another facility including long-term care	11.8 (5.3–18.3)	12.1 (11.1–13.1)	0.93	61,581 (35,515–87,647)	39,227 (35,234–43,219)	0.10
Court/law enforcement[b]						
Routine/birth/other	16.1 (14.6–17.6)	9.1 (8.9–9.3)	<0.001*	58,912 (52,255–65,569)	32,381 (31,570–33,192)	<0.001*
Admission type						
Emergency	13.6 (11.7–15.4)	11.0 (10.9–11.2)	0.008*	33,628 (23,773–43,483)	46,294 (45,436–47,151)	0.01*
Urgent	15.2 (13.1–17.3)	10.7 (10.5–10.9)	<0.001*	79,765 (70,875–88,654)	39,294 (38,260–40,328)	<0.001*
Elective	14.6 (12.5–16.7)	9.2 (8.9–9.5)	<0.001*	54,091 (45,521–62,660)	33,149 (32,064–34,234)	<0.001*
Newborn[b]						
Other[b]						
Aetiology						
Clostridial myonecrosis	12.8 (9.8–15.7)	11.2 (10.9–11.4)	0.29	19,249 (6,287–32,212)	38,599 (37,529–39,669)	0.004*
Non-clostridial myonecrosis	14.7 (13.5–16.0)	10.4 (10.2–10.5)	<0.001*	74,094 (67,852–80,336)	45,144 (44,468–45,820)	<0.001*
Site						
Extremity	15.8 (12.8–18.8)	13.2 (12.9–13.5)	0.09	74,265 (56,982–91,547)	54,092 (52,446–55,738)	0.02*
Truncal	19.3 (11.0–27.5)	14.6 (13.6–15.6)	0.28	110,244 (66,597–153,892)	63,425 (58,146–68,705)	0.04*
Mechanism						
Traumatic[b]						
Non-traumatic	14.4 (13.1–15.7)	10.5 (10.4–10.6)	<0.001*	21,029 (15,549–26,508)	53,911 (53,350–54,473)	<0.001*

* Statistically significant

[a] HCUP privacy protection requirements do not allow the reporting of data where there are less than or equal to 10 individual records in a given cell

too sick to withstand the therapy (e.g. patients with shock, mechanically ventilated patients). We were unable to test for this as the NIS database does not distinguish between shock preceding the initiation of HBO_2 therapy or shock that occurs after HBO_2 therapy has commenced. Indeed, APACHE scores are not recorded in the NIS database, thus it is not possible to address that question directly. However we feel that possibility is unlikely, since acute complications did not differ between groups. Moreover, our own practice is usually to keep sick patients ventilated between operative debridements and during HBO_2 therapy even when they could be extubated, in order to optimise oxygenation and tissue oxygen delivery.

Summary

To our knowledge, this is the largest study of the effects of HBO_2 therapy on patients with NSTI. Our study shows that patients with NSTI who received HBO_2 therapy had a lower mortality compared to patients who did not. The lower mortality was observed in the HBO_2 therapy group despite the fact that these patients were older and had a higher Deyo co-morbidity index. Patients who received HBO_2 therapy had a statistically significantly lower adjusted risk of in-hospital death. The results of this study add to the increasing body of evidence supporting the use of HBO_2 therapy in patients with NSTI. Certainly, there was no suggestion of harm from the use of HBO_2 therapy. To address this question more definitively a multi-centre randomised controlled trial may be required. However, this may prove to be difficult given the small number of patients with this condition in individual institutions [8]. In addition, given the strength of evidence supporting the use of HBO_2 therapy combined with antibiotics and surgery in clostridial myonecrosis and its high mortality, it has been suggested that where HBO_2 therapy is available it would be unethical to conduct a randomised controlled trial for this disease [14]. We conclude that even when taking into account the additional LOS and hospitalisation costs, the reduction in mortality associated with HBO_2 therapy justifies its use in NSTI.

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